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## Editorial

### ECONOMIC SECURITY AND PROFESSIONAL STANDARDS

HAPPINESS is largely dependent upon economic security. Financial difficulties interfere with development. Worry incident to the source of sufficient revenue to enable the student to devote himself wholeheartedly to his studies diminishes his capabilities for the future doctor.

In these days of world revolution the evolutionary process of standards is definitely threatened. No group is more threatened than the medical profession. Ethical standards, educational opportunities, and the relations of the profession to the public are in a state of flux.

Can we maintain the ideals which have characterized the development of our profession, or will we be caught in the maelstrom of the present world catastrophies? I believe that we can maintain our position with dignity and honor, but only by the greatest effort. The responsibility of the leaders at this time is particularly heavy. Precepts and examples are essential to the maintenance of ideals.

The doctors of the immediate future will become part of the great army to protect human rights and liberties. No greater privilege can come to any man than to participate in this struggle for the preservation of those democratic ideals set forth in our Constitution. In the confident hope that victory will crown our efforts let us not lose sight of what is being fought for. Many men will, when the struggle is over,

be satisfied to retain the financial security of the paternalism of government service. This very complacency on the part of the profession would inevitably lead to a socialized system of medicine.

It is urgent, therefore, that the teachers of medicine should urge upon the prospective doctor the importance of his normal relations to the public in the private practice of medicine. This relation should remain personal in character. To make of the *Doctor a Job Holder* would place the profession in a category unbecoming to the responsibilities involved.

Fortunately, in our country we divide the duties of the citizen into three categories: allegiance to God, Country and Family. Only one of these is collective—our duty to our native land; under the constitution the other two obligations are individual in character.

This basic triad differentiates democratic institutions from totalitarian philosophies. Cultivation of the ideals of individual responsibility is bound to strengthen a people, to increase initiative and lead to progress in every field.

The development of medicine is a record of individual endeavor. Inspired by the leadership of pioneers progress has been made and will continue to be made. Dreams, hopes and ambitions are the stuff out of which initiative and effort synthesizes progress. Controlled activity stifles initiative.

The pages of history record eloquently the names of men, not governments, whose efforts are responsible for the present noble positions in the diadem of world accomplishments in the profession of medicine. No revolution of any kind can ever efface the good accomplished by Hippocrates, De Chaulliac, Pare, Lister, Long, Morton, Pasteur, Percival and a host of individuals who did things.

Progress in medicine is bound up with individual effort and initiative sustained by ideals of service to the human family. The ideals of service must continue to stimulate the professional scion as well as the neophyte.

The teacher must never forget that his example is a pattern for his students. Nobility of purpose, devotion to duty and sympathetic understanding of the sick should characterize his every action. Personal aggrandizement and publicity are not qualities to be admired or condoned in teachers. It is well to be reminded of Emerson's epigram: "Character is above intellect."

In professional life the most desirable attribute is character. In order to maintain the character of the professional it is especially desirable that great care be

exercised in the acceptance of the mass of students who would be doctors. Adequate weeding out of undesirable students will eliminate those whose background is not sufficient to enable them to withstand temptations to which the lean years would expose them.

We are all familiar with the monstrous practice known as fee splitting. The cause of this pernicious habit must fundamentally be due to lack of character and lack of moral appreciation of the responsibility involved in the care of the sick. Bartering patients is a betrayal of trust. It is a means utilized by conscienceless and unscrupulous individuals who have gained entrance into the professional field. It is a prostitution of professional standards. With economic stress, one may expect to find that certain individuals or groups will stoop to low and unworthy practice. It is the duty of every one to see that betrayal of faith by some does not reflect on the honor and glory of our calling.

Maintainence of standards of conduct, insistence on proper appreciation by the public of the service of the profession and appreciation of our opportunities to serve the cause of human welfare, will bring contentment even in times of change.

ISIDORE COHN, M.D.



# Original Articles

## MANAGEMENT OF CEREBRAL TRAUMA\*

ELLIOTT C. CUTLER, M.D. AND

Mosely Professor of Surgery,  
Harvard Medical School

BOSTON, MASSACHUSETTS

ROBERT D. WHITFIELD, M.D.

Assistant in Surgery,  
Albany Medical School

ALBANY, NEW YORK

**T**HIS is a report of our experience with 396 consecutive cases of craniocerebral injury admitted to the Peter Bent Brigham Hospital during the years 1913 to 1939 inclusive. It concerns only the immediate management of the acute problem and does not represent fully the end result in this field. Only acute cases seen in this clinic within the first twenty-four hours have been included, and most of the patients were brought directly to the emergency room from the scene of the accident.

The one unvarying criterion for the acceptance of a case for review has been that the patient was unconscious following trauma. We have insisted that the record establish that the patient was either unconscious at the time of or after admission or was reported by a reliable observer to have been unconscious before admission. Other than this there has been no selection of cases whatsoever—all from the least to the most severe have been included. Careful consideration of the individual cases has shown that in a large proportion the degree of amnesia is greater and its duration considerably longer than the duration of unconsciousness.

We have been impelled to review these cases by the growing importance of the problem today. In the year 1936,<sup>15</sup> there were 110,000 fatal accidents in the United States of which 34 per cent were due to motor vehicles. Fifty per cent of the latter were craniocerebral injuries. The question

of the best management of these injuries during the acute phase is, therefore, one of pressing urgency.

There exists at present much difference of opinion as to the preferable management. For many years the primary consideration has been the control of the increased intracranial pressure consequent upon the injury. It has been recognized that the damage done to the cranial bones is of small moment unless these be driven inward or a compound fracture exists. The paramount consideration is the injury to the underlying brain. In this connection we wish to point out that injuries caused by rapidly moving objects, such as automobiles, are far more likely to result in damage to the intracranial contents than to the cranium, while those caused by slowly moving objects frequently result in a bursting type of injury with comparatively little damage to the brain and its coverings.

The problem of injury to the brain derives its peculiar qualities from the fact that this organ rests within a closed box surrounded by the tough fibrous dura matter and the filmy pia-arachnoid with the contained cerebrospinal fluid. The injured brain itself reacts in the familiar way in which all the bodily tissues react when damaged. The injury may be manifested simply by edema, by minute capillary hemorrhages, or by the formation of large hematomas with disruption of substance. If it were not for the incompressible

\* From the Surgical Clinic of the Peter Bent Brigham Hospital, Boston, Massachusetts.

space, the healing of the injured tissue would be simply the problem of repair, specialized as this is within the central nervous system.

But room must be made for the expanding brain at the expense of whatever may be dispensed with. Cushing,<sup>5</sup> many years ago, pointed out that during acute cerebral compression, certain definite changes occur in the clinical picture as the result of alteration in the blood flow within the cranium. These observations have been so repeatedly confirmed that they are generally accepted as of great prognostic significance in following a case of craniocerebral injury.

In the first stage of compression the blood supply to the vital centers in the medulla becomes gradually reduced to the point at which anoxemia of the circulatory and respiratory centers causes, through the vagus nerve, a slowing of the cardiac and respiratory rates. This is known as the period of *compensation*. In this stage there is a characteristic bradycardia and less often a slowing of the rate of respiration and vomiting. A complete physiological understanding of the mechanism of vagal response to anoxemia is wanting, but we know that, as anoxemia is induced, the vagus becomes more active, for once the heart rate has been depressed, section of the vagus brings about a more rapid rate. When the compression is further increased to the point where inadequate oxygenation of the medullary centers occurs, the pulse rate becomes still slower and the blood pressure begins to show a rise in the systolic and fall in the diastolic pressure. This is interpreted as a compensatory effort by the general systemic circulation. At this point the pulse rate tends to become alternately rapid and slow. Finally, when the period of decompensation is reached, the pulse rate, respiratory rate, and pulse pressure may simultaneously rise to progressively higher levels with eventual death. Associated with these phenomena is a rise in temperature, presumably due to the effect of the increased intracranial pressure on the temperature regulatory mechanism.

The essential feature is, therefore, the control of the increased intracranial pressure. There are three variable factors: One, to which we have already alluded, is the volume of blood within the cranium. The second is the volume of the cerebrospinal fluid. The third is the volume of the brain tissue itself.

The cerebrospinal fluid<sup>14</sup> is formed within the lateral ventricles by the choroid plexus. Its flow is thence through the foramina of Monro into the third ventricle, thence through the Sylvian aqueduct to the fourth ventricle and out through the foramina of Luschka and Magendie. Some fluid then circulates downward around the spinal cord and back to the great cisterns at the base of the brain. The flow from these is upward over the surface of the cerebral hemispheres to the arachnoidal villi through which readsorption takes place into the great venous sinuses.

The third variable factor is the volume of brain tissue itself. The acutely injured brain often becomes edematous, due to cellular reaction and extracapillary fluid, and its volume therefore increases. It is this increase, and in addition whatever increase is caused by the formation of hematomas, which is primarily responsible for the rise in intracranial pressure.

The whole problem of management lies in the ability of the surgeon to control one or more of these variable factors and therefore to keep the intracranial pressure reduced to a safe level. In the event of failure by conservative measures, removal of bone from the cranial vault accomplishes this purpose. This is usually done by removing the squamous portion of the temporal bone by the operation known as subtemporal decompression. Such a procedure must be performed before the cerebral ischemia has been long established, since few tissues are as sensitive to anoxemia as these.

In 1921, Weed and Hughson<sup>23</sup> proposed the use of hypertonic solutions to reduce intracranial pressure by the osmotic withdrawal of fluid from the edematous tissue.

At first hypertonic saline (sodium chloride) was utilized by intravenous infusion, but it was soon found that numerous petechial hemorrhages followed its use. Consequently 50 per cent glucose intravenously began to be used instead and was the agent of choice for many years. It was known, however, that a secondary rise in intracranial pressure occurred after its use, possibly due to glucose being absorbed by the brain tissue and thus reversing the osmotic flow.

In 1935, Gregerson and Wright<sup>9</sup> established the superior value of hypertonic sucrose for this purpose, and Jackson and his co-workers,<sup>11,12</sup> in 1937, reviewed the clinical use of this sugar when administered intravenously and reported excellent results. Theoretically, this is a more desirable agent than glucose because it does not pass the blood-brain barrier and there is no secondary rise of intracranial pressure. The efficacy of dehydrating agents has been seriously questioned by other workers, among whom are Browder and Meyers.<sup>4</sup>

In addition to the use of dehydrating agents intravenously, the limitation of fluid intake, with or without general dehydration by watery catharsis induced by magnesium sulfate orally or rectally, is widely practiced. Fay<sup>8</sup> reviews his results with this mode of treatment over a long period of time and reports a final mortality of 13.8 per cent. He points out that overdehydration is to be avoided.

In contrast to this is the vigorous hydration with repeated lumbar punctures practiced by Munro.<sup>17</sup> He avoids dehydration because he believes that the physicochemical equilibrium of the brain tissue is so severely upset by withdrawal of fluid and vigorous purging that more harm is done than good. If fluid intake is kept far above the normal daily intake, however, the intracranial pressure rises and other measures must be taken to control it. For this he uses repeated lumbar punctures.

Dandy<sup>6,7</sup> also eschews fluid limitation but does not force fluids above normal daily intake. He avoids dehydrating agents and vigorously condemns lumbar puncture,

even for diagnostic purposes. The reason for this condemnation is that there is inherent danger in lumbar puncture in the presence of increased intracranial pressure, unless the pressure is first relieved from above, because the brain may be so forced down into the foramen magnum by the existing pressure that a sudden release from below may jeopardize life. This contraindication is of sufficient importance in Dandy's mind to militate against the lumbar puncture even for diagnosis, since his experience has shown that careful observation of the patient's clinical condition will yield all the information available from diagnostic puncture. If in spite of rest the patient fails to improve, he advocates subtemporal decompression. Penfield<sup>19</sup> has voiced his objection to the use of lumbar puncture in patients with increased intracranial pressure, twisting the proponents of this point of view by calling them "picadors!" The danger is perhaps not widely appreciated.

Our own plan of treatment, in recent years at least, pursues a middle course. We view the problem of treatment as essentially one of restoring the normal physiological balance of the injured brain as early as possible. For this reason the paramount consideration is rest, which we seek to have consist of complete bed rest for one full week after all symptoms have disappeared. For the first few days after the injury we limit fluids moderately, usually to less than 1,500 cc. daily, occasionally to less than 1,000 cc. daily, with the occasional use of magnesium sulfate catharsis. However, we do not carry dehydration to the point at which systemic effects appear.

Patients in whom the diagnosis is doubtful, and all definitely, but slightly injured patients—in other words those who do not have greatly increased intracranial pressure—are submitted to lumbar puncture shortly after admission. The spinal fluid pressure is determined with the Ayer water manometer, no Queckenstedt test being performed, followed by withdrawal of 2 cc. of cell count and globulin determination by the Pandy

or ammonium chloride tests. We believe that when the lumbar puncture is carefully done by an experienced person, it is safe.

agement. Because of changes in the methods of therapy for this condition during this period of time, we have broken

TABLE I  
COMPARISON OF MORTALITY STATISTICS

	Cases	Mortality
Besley (1916) <sup>2</sup>	1000	53.0 %
Sharpe (1916) <sup>20</sup>	239	30.7%
Wilensky (1919) <sup>24</sup>	72	31.0%
Maarhead and Weller (1921) <sup>15</sup>	100	26.0%
Stewart (1921) <sup>21</sup>	6135	52.0%
AUTHORS (1913-1921)	63	26.98%
Bower (1923) <sup>3</sup>	62	26.1 %
Heuer (1924) <sup>10</sup>	223	35.8 %
Kennedy and Wortis (1926-1929) <sup>26</sup>	1000	37.8 %
Beekman (1921-1926) <sup>1</sup>	331	11.4 %
McClure and Crawford (1927) <sup>13</sup>	441	14.7 %
AUTHORS (1922-1930)	93	11.83%
Swift (1935) <sup>22</sup>	112000	25.0 %
Munro (1930-1933) <sup>16</sup>	1450	17.5 %
Fay (1927-1932) <sup>8</sup>	528	20.0 %
Woodhall (1936) <sup>25</sup>	300	18.66 %
AUTHORS (1931-1939)	240	7.92%
AUTHORS (Total 1913-1939)	396	11.87%

Severely injured patients, however, are not submitted to lumbar puncture until the immediate danger is passed. X-ray films of the skull are taken at some time during the patient's hospital stay for medicolegal reasons; but unless palpation raises the question of a depressed fracture of the skull, the taking of x-ray films is delayed until the patient's condition has been stabilized.

So far we have discussed only uncomplicated concussion and contusion of the brain. In the event that definite evidence of acute extradural or subdural hemorrhage is present, or if there is a compound fracture of the skull, operative intervention has been our practice in common with other clinics.

The subsequent tables demonstrate the material studied, the methods of therapy and immediate results achieved.

#### GENERAL MORTALITY STATISTICS (TABLE I)

Table I reviews the general statistical evidence in the field of cerebral trauma between the years 1913 to 1939, that is, the period in which we have studied its man-

down the evidence by nine-year periods. In Table I our own figures are set up in comparison to the figures submitted by authors working on this problem in the corresponding nine-year period. Note that in the first nine-year period, 1913 to 1921, the mortality figures vary roughly from 25 to 50 per cent. This was a period characterized by the greater use of the surgical means of treatment than is now generally advocated. When one comes to the second nine-year period, 1922 to 1930, the mortality figures are all substantially lower, varying from 11 to 37 per cent. During this interval as a whole the surgical treatment of all patients with intracranial damage came into discredit with a large fragment of the medical profession, and possibly a further factor in the reduced mortality rate was the reintroduction of dehydration as a method of therapy. When we come to examine the last nine-year period, 1931 to 1939, we notice again a further falling off in the mortality rate. There may be several factors which caused this reduction: (1) A further diminution in the amount of surgery performed; (2) a more widespread use of dehydration methods, and finally (3) a

realization both by the people and the profession of the seriousness of cerebral damage, a large proportion of which occurs

tomas and compound fractures of the skull. The mortality in the period 1913 to 1921 inclusive was 26.98 per cent. This fell to

TABLE II  
MATERIAL AND MORTALITY

YEARS	Group A		Group B		Group C		Total	
	Cases	Mortality	Cases	Mortality	Cases	Mortality	Cases	Mortality
1913-1921	18	2*	25	1*	20	14	63	17
	28.57%	11.1%	39.68%	40%	31.75%	70%		26.98%
1922-1930	39	0	36	0	18	11	93	11
	41.94%	0%	38.71%	0%	19.35%	61.1%		11.83%
1931-1939	110	0	89	3+	41	16	240	19
	45.83%	0%	37.08%	3.4%	17.08%	39.0%		7.92%
Total	167	2	150	4	79	41	396	47
	44.41%	12%	37.88%	2.6%	22.73%	51.9%		11.87%

\* Due to non-cerebral causes  
+ Two of these due to non-cerebral causes

in automobile accidents. A good many more patients suffering from the less serious types of intracranial damage were hospitalized and therefore available for study. It was the considerable drop in our own mortality statistics and the discovery that our figures were now perhaps lower than those usually reported that led us to present this study at this time. The drop in our own mortality from 26.9 per cent in the first period to 7.9 per cent in the last period is significant and has led us to try to evaluate the reason for this.

#### AUTHOR'S MATERIAL AND MORTALITY STATISTICS (TABLE II)

In Table II we have attempted a more complete analysis of our own material, again breaking the periods for study into nine-year intervals in order that any change in therapy might be evaluated if a significant drop in the mortality rate occurred. For each nine-year period we have broken down figures into separate groups according to the severity of the damage as already outlined. Group A includes those unconscious for less than fifteen minutes; group B those unconscious from fifteen minutes to twenty-four hours, and group C, the seriously damaged patients, those unconscious longer than twenty-four hours as well as those with extradural and subdural hema-

7.92 per cent in the period 1931 to 1939 inclusive in spite of a rise in the total number of cases from sixty-three for the first period to 240 for the last. During this time, however, the relative proportion of severely injured patients fell sharply from 31.75 per cent in 1913 to 1921 to 17.08 per cent in 1931 to 1939. But the mortality in the severe cases has remained consistently well above 40 per cent until 1931 to 1939 when it fell to 39 per cent. The drop in the percentage of severe cases is only of fairly probable mathematical significance as the difference lies between two and three times its standard error, whereas the decrease in the gross mortality percentage is over four times its standard error, and the decrease in the mortality percentage of the severe cases is five times its standard error. Thus the decreases in the mortality percentage are of definite unequivocal mathematical significance.

#### SURGICAL THERAPY (TABLE III)

In Table III we have attempted to evaluate the efficacy of surgical therapy. During the first nine years of the study its incidence was above 52.38 per cent, whereas it has since then fallen sharply, dropping to 15.05 per cent during the period 1922 to 1930, and then to 13.75 per cent in 1931 to 1939. In the earlier years many of the

moderately injured group were operated upon. At the present time our indications for operation are: (1) Increasing coma after

patients did not occur until nine years later and must be related to factors other than surgical therapy.

TABLE III  
SURGICAL TREATMENT

YEARS	Exploration or Decompression	Elevation Depressed Fracture	Encephalography or Ventriculography	Total Operations	Total Cases	% Operations	% Total Mortality	% Severe Cases	% Mortality Severe Cases
1913-1921	29	4	0	33	63	52.38	26.98	31.75	7.00
1922-1930	9	5	0	14	93	15.05	11.83	19.35	6.11
1931-1939	21	7	5	33	240	13.75	7.92	17.08	3.90
Total	59	16	5	80	396	20.20	11.87	22.73	5.19

a period of several hours observation; (2) the appearance of focal neurological signs indicating a rapidly growing extradural or acute subdural hematoma; (3) failure to improve after forty-eight hours of conservative treatment; (4) compound fractures of the skull, which are immediately débrided and sutured, depressions being replaced at the same time (other depressed fractures are not operated upon until the recovery period is fairly well advanced). We are here referring, of course, to cranial operations. Surgical intervention for other traumatic injuries takes place at the time imposed by the urgency of the indications.

The operation most often performed has been subtemporal decompression. If focal signs were present, it was of course performed on the side indicated; if they were not, the right side was always elected in right-handed persons. In a considerable number of instances, bilateral subtemporal decompressions were done, and in a few patients with considerable evidence of advanced pressure with marked medullary embarrassment suboccipital decompressions were chosen.

It is noteworthy that the significant drop in the percentage of operations performed occurred at the same period as the significant drop in the gross mortality percentage and undoubtedly has a bearing upon it, whereas the significant drop in the mortality percentage of the severely injured

#### DEHYDRATION THERAPY (TABLE IV)

Dehydration first began to be employed in 1922 shortly after the value of dehydrating agents in patients with increased intracranial pressure was pointed out. Magnesium sulfate orally or rectally has been used since that time, but other agents, such as intravenous glucose and sucrose, have been employed only six times in the last six years. At no time, however, have more than 36 per cent of the total number of admissions in the series received these drugs. The incidence of use has risen from 20.43 per cent in 1922 to 1930, to 31.67 per cent in 1931 to 1939.

Associated with this has been limitation of fluid intake since 1925. No figures are available in the records as to the fluid intake before that date. There is a definite tendency since that date toward stricter dehydration by limitation of fluid intake. In the period 1925 to 1930 only 15.38 per cent of those patients on whom a record of fluid intake is available received less than 1,000 cc. daily and 46.15 per cent over 1,500 cc. In the period 1931 to 1939, however, these respective figures are: 32.91 per cent below 1,000 cc., 36.18 per cent between 1,000 and 1,500 cc., and 30.92 per cent over 1,500 cc. In short, at the present time 69 per cent of these patients have some limitation of fluids. The remainder, on whom no figures are available, are those who were detained only twenty-four hours or less,

and all come within the mildly injured group, save for an occasional patient who died shortly after admission.

cerebral trauma, particularly in a clinic where the responsible surgeon often has no opportunity personally to verify the fact of

TABLE IV

EFFECT OF DEHYDRATION

## A Magnesium Sulphate by Mouth or Rectum

Years	Total Cases	Number Cases in which used	% Cases In which used	% Total Mortality	% Group C Cases	% Mortality Group C
1913-1921	63	0	0	26.98	31.75	70.0
1922-1930	93	19	20.43	11.83	19.35	61.1
1931-1939	240	76	31.67	7.92	17.08	39.0
Total	396	95	23.99	11.87	22.73	51.9

## B Restriction of Fluid Intake

Years	Total Cases	Number Cases Fluid Restricted	% Cases 1000- 1000cc	Above 1500cc	% Total Mortality	% Severe Cases	% Mortality Severe Cases	
1913-1921	63	0	0	0	26.98	31.75	70.0	
1922-1930	93	26	4 4.30%	10 10.75%	12 12.90%	11.83	19.35	61.1
1931-1939	240	152	50 20.83%	55 22.92%	47 19.58%	7.92	17.08	39.0
Total	396	178	54 30.34%	65 36.51%	59 33.14%	11.87	22.73	51.9

The differences in the percentage of cases in which strict and moderately strict dehydration was employed are in all instances greater than twice the standard error of the difference, and with one exception all are from five to ten times that standard error. Therefore, the increasing use of this method of treatment in our series is mathematically true and may be correlated with the drop in the mortality percentage, both gross and with regard to the severely injured patient.

## USE OF LUMBAR PUNCTURE (TABLE V)

Throughout the series the use of lumbar puncture as a diagnostic procedure has held a significant place which has increased in frequency. In the period, 1913 to 1921, it was employed in 32 per cent of the total admissions; while in 1931 to 1939 75 per cent were submitted to it. Indeed in recent years it has become increasingly difficult to emphasize to the house staff that the presence of erythrocytes in the cerebrospinal fluid is of somewhat less importance than a definite history of unconsciousness and the presence of retrograde amnesia. We believe, however, that the procedure offers valuable confirmatory evidence of cranio-

unconsciousness, especially if this be short-lived. Moreover, as carried out here we believe it to be safe. In the severely injured patient it is undertaken only on the direct and personal authorization of a senior resident or a member of the senior staff; in the mild cases, the emergency ward man or ward house officer routinely performs it, but only as restricted by a definite method.

This increase in the percentage of cases in which diagnostic lumbar puncture was employed is mathematically significant, for it is seven times its standard error. Since it was associated with a significant drop in the mortality percentage, we may say that the procedure is safe. Obviously a diagnostic procedure such as this cannot contribute directly to that reduction.

Lumbar puncture as a method of treatment we mention only to decry it. It was first so used here in 1922. The incidence of its use rose from 0.0 per cent in the period 1913 to 1921, to a maximum of 11 per cent in 1922 to 1930, falling to 3 per cent in 1931 to 1939. There is at least one fatality (1923, Surg. No. 18910) directly attributable to its use. This patient, though moderately severely injured, presented a vivid and sudden change for the worse immediately

following the withdrawal of 25 cc. of bloody cerebrospinal fluid, showing rapidly increasing medullary embarrassment.

injured patients and in a considerable number of the severely injured.

3. Traumatic shock, if present, is in-

TABLE V  
USE OF LUMBAR PUNCTURE

YEARS	Diagnostic	Therapeutic	% Mortality Group C
1913-1921	20 32%	0 0%	70
1922-1930	16 17%	10* 11%	611
1931-1939	180 75%	6 3%	390
Total	216 55%	16 4%	

\* One fatality in this group

The differences between the percentage of use of the therapeutic lumbar puncture in the middle period of the study and that in either the first or last period are mathematically significant, being over eight times the standard error. There is no significant difference between the first and the last period. The eventual abandonment of this method occurred simultaneously with the drop in the mortality percentage of the severe cases.

#### PLAN OF TREATMENT

During the early years of the period covered by this study most patients admitted with craniocerebral injuries were cared for on the general surgical service, the essentially separate neurosurgical service seeing those who seemed to need operative intervention. Since 1932, all these patients have been the direct responsibility of the senior author, and have been cared for by him with the assistance of the assistant resident surgeon assigned to him personally. In this period a definite plan of treatment has been adopted.

The essential points of this are as follows:

1. All patients with a definite history of unconsciousness or amnesia following an accident are hospitalized.

2. Diagnostic lumbar puncture is performed in all the mildly and moderately

variably treated before the patient is moved from the emergency room to the ward.

4. X-ray films of the skull, while made in every case for medicolegal reasons, are postponed until the added trauma of extra handling and moving will no longer adversely affect the patient.

5. Rest in bed for one week after subsidence of all evidences of increased intracranial pressure with gradual resumption of activity thereafter.

6. Mild dehydration for three days, rarely longer.

7. Operative intervention for the definite indications previously mentioned.

#### SUMMARY

1. We have reviewed a series of 396 consecutive cases of craniocerebral injury admitted to the Peter Bent Brigham Hospital during the years 1913 to 1939 inclusive, of which 44.41 per cent were mildly injured, 37.88 per cent moderately injured, and 22.73 per cent severely injured.

2. The gross mortality for the entire series was 11.87 per cent; for the mild cases, 1.2 per cent; for the moderately injured cases, 2.6 per cent; and for the severely injured cases, 51.9 per cent. The mortality for all cases has decreased from 26.98 per cent in 1913 to 1921 inclusive, to 7.92 per

cent in 1931 to 1939 inclusive, but in the severely injured cases has remained constant.

3. The incidence of operative intervention has been reduced from 52.38 per cent to 13.75 per cent from the former period (1913 to 1921) to the latter period (1931 to 1939).

4. Mild dehydration therapy has been employed with steadily increasing frequency. From 1931 to 1939 inclusive 42 per cent of patients had some limitation of fluid intake and 31.67 per cent received large doses of magnesium sulfate orally or rectally.

5. Diagnostic lumbar puncture has been utilized more and more frequently, up to 75 per cent of all cases from 1931 to 1939 inclusive; therapeutic lumbar puncture has been abandoned.

6. A general plan of treatment as used by us at present is described.

### CONCLUSIONS

The treatment of craniocerebral injuries by complete rest, and an attempt to restore the physiological equilibrium as quickly as possible are shown to be safe and efficient means of managing these injuries. Accurate history, painstaking examination of the patient and conscientious observation of his course are absolutely essential. Judicious use of lumbar puncture as a diagnostic aid is often advantageous, but its therapeutic use is to be condemned. Mild dehydration during the period of immediate recovery is helpful but should not be carried to excess. Operative intervention is necessary in a small number of cases but only on definite indications; the surgeon, however, should be prepared to offer it when indicated and not be misled into conservative management beyond the point of safety.

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# ACUTE INTUSSUSCEPTION IN INFANCY\*

A. J. CAPONE, M.D.

Assistant Visiting Surgeon, Somerville Hospital

SOMERVILLE, MASSACHUSETTS

THE purpose of this paper is to emphasize the diagnostic points of acute intussusception, to review the literature regarding the nonoperative and operative treatment with their advantages and to present several personal cases that have received treatment.

## DIAGNOSIS

The diagnosis made on a careful history obtained from the mother, who usually relates that the child was perfectly well and healthy until seized by a sudden, acute pain that caused the child to cry vigorously, but that the baby would have spells of entire quiet from five to ten minutes between paroxysms; that there were one or two normal bowel movements followed by bloody mucus resembling currant jelly. Vomiting occurred early and was a prominent symptom.

A physical examination may reveal a child that does not seem acutely ill when seen early, and especially if seen between paroxysms. There is no rise in temperature, skin may be moist and cold, pulse rapid, abdominal examination may find it relaxed with tenderness and moderate spasm to the right lower quadrant with or without finding of a doughy tender mass that is movable.

Rectal examination is to be emphasized as being most important since the finding of blood on the examining finger is practically a criterion of this condition. One must note, however, that the most common error is to regard the case as one of gastroenteritis, the physician's attention being engrossed by the vomiting and bloody stools. X-rays have been employed in substantiating the diagnosis since a barium enema may demonstrate a narrowing or a complete blockage at the ileocecal valve.

## DIFFERENTIAL DIAGNOSIS

One must consider acute appendicitis, enterocolitis, rectal prolapse, a bleeding Meckel's diverticulum, and lastly, abdominal Henoch's purpura.

1. *Acute Appendicitis.* Here there is fever, spasm, elevation of white count; the onset is not as acute as in intussusception and the history of shock is not obtained as regularly. There is usually nausea for a day followed by abdominal pain. In appendicitis there is no mass early; if there be a mass, it would appear in a week or ten days after the acute attack and would represent localized appendiceal abscess. It is a known fact that acute appendicitis under the age of two is uncommon.

2. *Enterocolitis.* This condition rarely has the sudden onset of intussusception and it is associated with an excessive number of loose watery stools with or without mucus and blood. Here feces and flatus continue to pass and this is not the case in obstruction of intussusception. No mass is palpable. There is no paroxysm of pain as one would see in intussusception. If there be vomiting, it is much less than in intussusception and is not associated with other symptoms of developing obstruction. It is wise to note, however, that enteritis with its hyperperistalsis may lead to intussusception.

3. *Rectal Prolapse.* This condition is in itself easily recognizable by the rectum coming into view. It may be easily differentiated from a prolapsed intussusception by the fact that one cannot pass a finger into the rectum alongside the protruding mass if it is a rectal prolapse.

4. *Meckel's Diverticulum.* The history is somewhat similar to that of appendicitis; the temperature is elevated along with the

\* From the Department of Surgery, Somerville Hospital, Somerville, Massachusetts.

white blood count. Here, however, one must note that a Meckel's diverticulum is one of the predisposing causes of an intussusception.

*5. Abdominal Henoch's Purpura.* Differentiation in this condition may be difficult inasmuch as in abdominal purpura one may have a sudden onset with severe pain and associated shock along with the passage of blood per rectum and frequently the presence of an abdominal mass due to subserous extravasation of blood along the bowel. The differentiation would be noted as follows since the symptoms of abdominal Henoch's purpura are: (a) A purpuric rash over the body, most frequently on the extensor surfaces of the extremities; (b) a good test is to apply a tourniquet to the arm for a few minutes to produce distal petechial hemorrhages; and (c) low platelet count.

#### TREATMENT

There are two schools of thought regarding treatment: (1) nonoperative followed by surgery if not successful, and (2) operative treatment as soon as the diagnosis is determined.

*Nonoperative Treatment.* Hipsley, of Australia, has reported in many articles over 200 cases. His method is to employ hydrostatic pressure of saline solution into the rectum since he believes that 60 per cent of cases can be reduced with this technic which is briefly as follows:

The infant is given a general anesthetic. A No. 16 catheter is placed up high into the rectum and both buttocks are pinched over the catheter so as to prevent any reflux of fluid. The irrigating can is placed three to four feet above the patient and one quart of saline solution is allowed to run in by gravity. The pressure is held in this manner for three minutes, then allowed to escape. This procedure is repeated several times. Hipsley notes that the abdomen should not be palpated while the fluid pressure is on because of the danger of rupturing the weakened intestinal wall. The difficulty is to be sure of complete reduc-

tion of the intussusception and he gives the following as evidences of reduction:

1. *Abdominal distention* following the giving of the enema demonstrates that the fluid has passed into the small bowel past the tumor with resultant reduction of the mass.

2. *Alteration in the Circumference of the Abdomen.* A successful reduction of the tumor mass shows an increase of approximately two inches about the umbilicus after the reduction.

3. *Yellow Fecal Material in the Returned Saline Solution.* The first or second return of saline solution may demonstrate some amount of blood. If after these first injections, there is a return of fecal material, it clearly demonstrates that this has come down proximal to the tumor mass.

4. *Flatus in the Return.* This likewise would demonstrate reduction of the tumor mass since the flatus would necessarily have to come proximal to the mass. X-ray filling of the small intestine after an opaque injection of barium has been used instead of saline. Here the presence of barium in the small bowel clearly indicates a reduction.

5. *The Use of Charcoal to Verify Reduction.* In an infant seen during the early stage of this disease where there is considerable doubt as to the diagnosis, one could easily ascertain whether or not there is obstruction at any point along the bowel tract by giving the child a teaspoonful of powdered charcoal mixed in a half ounce of water by mouth. Normally, this will be passed by rectum from within five to seven hours if there is no obstruction.

Hipsley notes that he continues the treatment with surgery if he is not certain of complete reduction, and states that he never employed this treatment after twelve hours of the acute seizure.

Retan and Stephens further elaborate the hydrostatic pressure treatment of Hipsley by introducing rectally a barium mixture and observing its action under the fluoroscope. The method is as follows:

The barium mixture is introduced with minimal pressure until the colon is filled to

the advancing point of the intussusceptum (the enema source is held between two and three feet above the level of the patient);

definitely established even if the procedure fails. This type of reduction is particularly valuable in the first twelve hours.

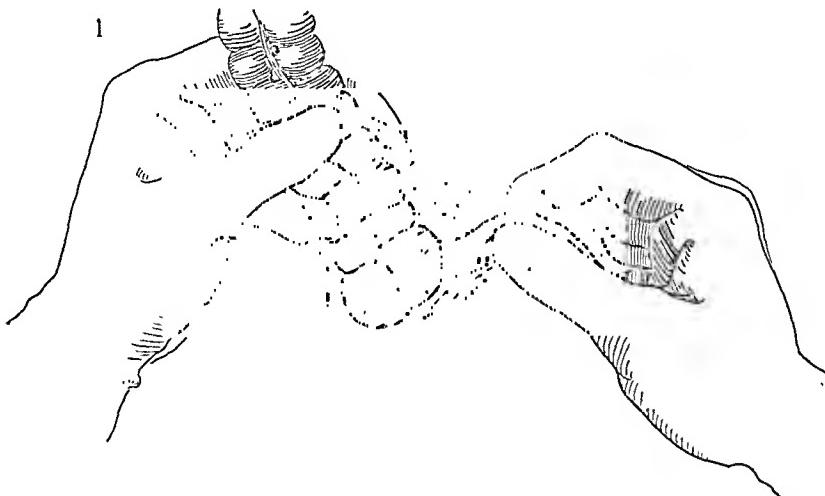


FIG. 1. Method of manual disinversion. Here the intussuscepted bowel is milked out while gentle taxis is employed on the invaginated portion.

then with the pressure gravity shut off, the barium is forced against the intussusceptum by manual pressure externally on the already filled colon under visual guidance and control. As the intussusceptum recedes, more of the mixture is introduced and the manual pressure again applied. As soon as the intussusception seems reduced the colon is completely filled by gravity pressure to make certain that the reduction is complete; if such is the case, the colon fills completely and the barium mixture can be seen passing into the terminal ileum. These fluoroscopic observations are immediately checked by roentgenograph.

Retan lists the following as evidences of reduction: (1) The colon will fill completely with leakage of barium into the ileum as evidenced under the fluoroscope and confirmed by an x-ray photograph. (2) The abdominal tumor will disappear. (3) The child is relieved of all symptoms of shock, pain, vomiting, etc.

Retan and Stephens state that the advantages of attempting to reduce an intussusception under the fluoroscope are that this method is intelligent, scientific, safely conservative, and the diagnosis is

#### OPERATIVE TREATMENT

The majority of men in this country do surgery from the beginning. Several operative procedures are employed. A right, lower quadrant, rectus retracting incision is the one of choice, although some favor a low midline incision since there is less bleeding encountered and permits access to both right and left portions of the abdomen. In the early cases after the opening of the abdomen and localization of the tumor mass, the milking of the tumor mass is enough, accompanied by warm compresses to reduce swelling. (Fig. 1.) The first part of the reduction is usually easy and may be accomplished by holding the gut firmly with one hand just below the advancing point, and then sliding the thumb and forefinger of the other hand along the sheath, pushing the intussusceptum in front. The last few inches of the reduction are sometimes difficult, and it is here unsafe to put much traction on the gut. The cause of difficulty is usually edema of the gut and mesentery, and perseverance will frequently diminish the edema enough to allow a reduction which at first seemed impossible. At this point it

is wise to note that an appendix delivered from an intussusception is so distended by edema that at first glance it may look as

mass, some form of resection must be attempted. In such a case the simplest procedure is to perform a Mikulicz obstruc-

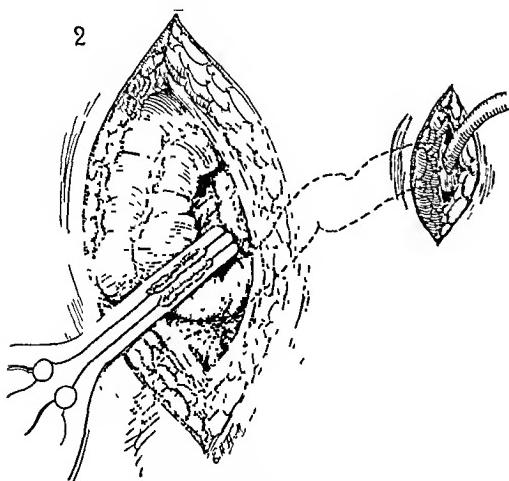


FIG. 2. Obstructive Mikulicz resection of the gangrenous intussusception by a double clamp. Ileostomy performed six inches from resection for purpose of immediate drainage of bowel tract.

though the patient had acute appendicitis. It is very unwise to add an unnecessary appendectomy to a situation already precarious.

When, however, resection becomes absolutely necessary on account of reduction being impossible or because of gangrene, there are many methods to choose from, although they are accompanied by a high mortality rate: (1) Resection with end to anastomosis or an end to a lateral anastomosis; (2) resection with a double enterostomy according to the technic of Mikulicz; (3) lateral anastomosis about the lesion with a secondary resection later if the condition of the child permits; (4) ileostomy with a secondary resection later; (5) lateral anastomosis about the lesion with secondary sloughing and healing. (6) resection of the intussusceptum through an incision in the intussusceptions with or without a lateral anastomosis; and (7) incision in the wall of the intussusceptiens to permit wound reduction, followed by one of the aforementioned methods if necessary.

If exploration reveals an irreducible gangrenous mass, or a nonviable reduced

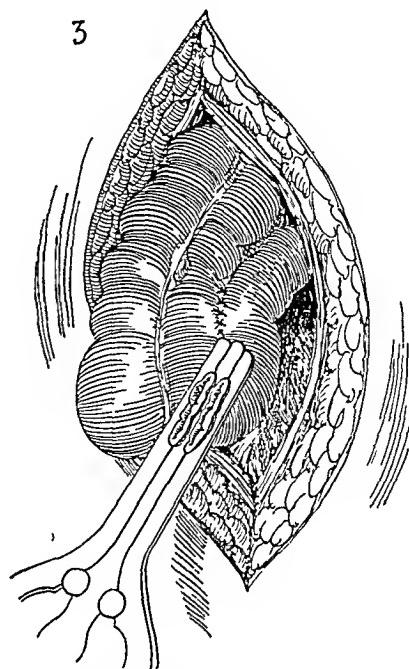


FIG. 3. Mikulicz resection of the gangrenous intussusception with a side-to-side anastomosis between the terminal ileum and proximal colon according to procedure of Barnes Woodhall, who believes that there is less fluid loss with this method.

tive resection with a temporary ileostomy eight inches from the ileocecal valve through a small stab incision. (Fig. 2.) This immediately relieves the obstruction and enables one to re-establish the bowel continuity by the ileocolic septum some seven to ten days later.

Woodhall, in 1938, reported several operative cases in which his technic was to do a lateral anastomosis around the lesion followed at the same operation by the usual Mikulicz procedure. (Fig. 3.) He states that in addition to guaranteeing immediate continuity of the bowel lumen, this technical modification has proved distinctly valuable in controlling the resultant intestinal obstruction and fluid loss.

#### CASE REPORTS

The first two patients were treated by staff surgeons of the Somerville Hospital;

the last three were personal cases of the author.

CASE I. No. 40547. S. B., a male infant of seven months, was admitted to the hospital June 15, 1934, with a history of sudden attack of pain with vomiting twenty-four hours before. An enema given by the mother two hours after the first attack showed free blood. The child vomited everything taken by mouth since and had had two free black stools. Examination revealed the baby to be restless as if in pain. The temperature was 101°F. rectally, the pulse was very rapid, ranging from 140 to 160, white blood count 17,000. The abdomen was distended and there was a small mass at the left upper quadrant. Free blood was present on rectal examination and the child was prepared for operation. Clysia of 150 cc. saline was administered.

A left midrectus muscle retracting incision was made. An intussusception, composed of three inches of terminal ileum into ileocecal valve was brought up into the incision and easily reduced manually. The terminal ileum was edematous but not gangrenous. Because of distended loops of bowel, a cecostomy was made. The abdomen was sutured in layers with the cecostomy catheter brought out at the lower end of the incision. A clysis of 200 cc. saline was given postoperatively and the child's condition was good.

On June 16, 1934, the temperature was 104°F. rectally, the abdomen was badly distended and the cecostomy catheter was draining. A small Levin tube was passed intranasally into the stomach and adequate fluids were administered by clysis.

On June 17, 1934, his condition was unimproved. The temperature was 104°F. rectally, pulse, 160, and there was a free movement of bloody mucus. The distention of the abdomen remained the same.

On June 18, 1934, the infant seemed improved; his temperature was 102°F. rectally, and he retained small amounts of liquids by mouth. The abdominal distention was less. At 11:30 P.M. the child developed a high respiratory rate of 64 and expired at 3 A.M. the next morning.

CASE II. No. 64780. A. C., a female infant of five months, was admitted to the hospital January 28, 1941, at twelve noon. There had been sudden, acute pain followed by vomiting

thirty-four hours before admission. This was followed by a good bowel movement and apparent relief although there were repeated attacks of pain and vomiting. Between attacks the child seemed quite comfortable. There was rectal bleeding noted eight hours before admission. The baby was then seen by a physician who made the diagnosis of intussusception.

Preoperative examination revealed a dehydrated, five-months old baby with knees flexed; temperature, 98.6°F. rectally; pulse, 140; urine negative. Abdominal examination revealed a palpable mass in the right lower quadrant. Rectal examination revealed much free blood. The prognosis was grave in view of the duration from the first attack. It was believed that gangrene was present and the child was prepared immediately for operation. Two hundred cc. 5 per cent glucose in saline were given by hypodermoclysis.

Under ether anesthesia a right rectus, muscle retracting incision was made. The abdomen was opened and revealed a large intussusception of about ten inches of terminal ileum into the ileocecal valve that was reduced manually with great difficulty especially at the last two inches of ileum that were bound down into the cecum. The intussusceptum was black with gangrene extending up into the mesentery. As this portion of the gut was not viable, an aseptic end-to-end anastomosis was made bringing together the ileum and cecum. An ileostomy tube was inserted one foot proximal to the anastomosis. The immediate postoperative condition seemed good. Another clysis of 200 cc. 5 per cent glucose in saline was administered. The condition appeared good until 11 P.M. when the child suddenly developed a high respiratory rate and expired.

CASE III. No. 61455. K. P. G., a male, aged four months, was admitted to the Somerville Hospital at 9:30 A.M. on April 25, 1940. The history showed that the child had been perfectly well and healthy since birth but that two days before admission he was seized with a sudden pain followed by vomiting. The mother stated that his bowels moved freely after the acute onset, but that for the past twenty-four hours there had been some blood passed rectally. She also stated that the baby was very "colicky" from the previous day and that there was a gradual distention of the abdomen. The baby vomited all food given since the attack but there was some retention

of water given orally. The child was first seen by a physician on the morning of hospital admittance and immediately transferred for surgical attention.

Physical examination revealed a well developed and well nourished male infant who was listless, but did not seem to be in acute distress. The skin was dry and he was lying on his back with knees flexed. The temperature was  $100.8^{\circ}\text{F}$ . rectally, pulse 132, respirations 30, white blood count, 21,800. Urine was concentrated with slightest possible trace of albumin. The pupils reacted to light; eardrums were normal; the tongue was dry and coated; there was no neck stiffness and no cervical adenopathy. Heart sounds were normal and lungs were clear throughout.

The abdomen was distended but soft. Careful palpation did not reveal a mass. Palpation at the right lower quadrant caused the child to cry; a moderate spasm was felt at this point.

Rectal examination revealed no mass but a good amount of bloody mucus gushed forth on withdrawing the examining finger.

Because of the finding of blood in the rectal examination and noting the history, the infant was operated upon immediately. The operation was performed one hour after admission to the hospital. A clysis of 200 cc. 5 per cent glucose in saline was given into the thighs prior to operation.

Under ether anesthesia, palpation of the abdomen did not reveal a tumor. The abdomen was opened with a right, rectus muscle, retracting incision. On opening the peritoneum the intussusception immediately came into view. The site of intussusception was the ileocecal valve and six inches of ileum were invaginated into the cecum. This was reduced by milking it out manually; the invaginated portion was very dark and much reddened but not actually necrotic. The ileum was fixed to the cecum by two gastro-enteric sutures to prevent recurrence. The abdomen was closed without drainage, and the immediate postoperative condition was good.

The child was returned to the ward and kept warm. Another clysis of 200 cc. 5 per cent glucose in saline was given into the thighs postoperatively. Another clysis of 100 cc. was given at 3:30 P.M. and at 8:00 P.M. The infant was quieted by the administration of ten drops of paregoric orally every three hours. He began to retain water by mouth in two and three

ounce amounts eight hours after operation and a milk formula the next day. Convalescence was smooth, except for an elevation of temperature to  $103^{\circ}\text{F}$ . rectally on the second day, which subsided by lysis by the fifth day. A stitch abscess was opened on the seventh day. He was discharged with the incision well healed on the ninth day.

CASE IV. No. 64431. M. De B., a male, aged six months, was admitted to the Somerville Hospital on December 28, 1940. The baby was well until 5 P.M. on the day of the admission, when he was seized with acute pain followed early by vomiting which was persistent. He was seen at home at 8 P.M.

Physical examination revealed a well developed and well nourished male infant, lying on his back with knees flexed, crying vigorously during paroxysms, but entirely quiet for three to five minutes between paroxysms. The temperature was  $98^{\circ}\text{F}$ . rectally, pulse, 110, respirations 28; skin moist, white blood count, 9800.

The routine examination was negative except for tenderness and moderate spasm at the right lower quadrant. The abdomen was otherwise soft with no distention. No tumor was felt. Rectal examination revealed a bloody discharge on withdrawal of the examining finger. Because of this latter finding a diagnosis of acute intussusception was made and the child was taken to the Somerville Hospital for operation. The infant was prepared preoperatively by administration of a clysis of 200 cc. 5 per cent glucose in saline into the thighs.

Under ether anesthesia a right, rectus muscle, retracting incision was done. On opening the peritoneum there immediately came into view a large sausage-like mass with bluish discoloration; this mass composed the terminal ileum, appendix and cecum invaginated into the ascending colon for a distance of three inches. This intussusception was milked out manually and revealed the intussusceptum to be very edematous and discolored but not necrotic. The abdomen was sutured in layers. The immediate postoperative condition was good. A clysis of 100 cc. of 5 per cent glucose in saline was given into the thighs postoperatively. After ether recovery the child maintained fluid given by mouth. His regular milk formula was given on the following day. The convalescence was smooth and the child was discharged on the eighth day with a well healed incision.

CASE V. No. 65126, A. Le B., a male, aged six months, was admitted to the Somerville Hospital on March 1, 1941. The mother stated

Although this child did not have typical symptoms of intussusception as far as acute onset, pain and vomiting were concerned, it



FIG. 4. X-ray proving the absence of intussusception. The large bowel fills completely with the barium enema. There is no deformity of the cecum, and no incompetency of the ileocecal valve.

that the child had a bowel movement that was streaked with blood twenty-four hours previous to admission. She further stated that she afterward gave the child some milk of magnesia and when no further bowel movement occurred she placed a finger in the baby's rectum which showed some blood. The child had vomited two of his feedings. At no time previous to his hospital admittance did he seem to have any abdominal pain.

Physical examination demonstrated a very well developed and well nourished child, lying on his back with legs extended, temperature was 99.6°F. rectally, pulse 120, respirations 32, white blood count 7,750; urine examination was negative. Ears, eyes, nose, throat, heart and lungs were negative.

The abdominal examination revealed no distention but showed some tenderness through the whole lower portion of the abdomen on palpation. Rectal examination showed a small amount of old blood on the examining finger.

It was believed that there was a possibility of this condition and that a barium enema x-ray would demonstrate whether or not there was any obstruction along the large bowel tract. The barium enema revealed a complete filling of the large colon, no incompetency of the ileocecal valve and a filling of the terminal ileum. (Fig. 4.) In view of this the possible diagnosis of intussusception was dismissed. The child did well during the hospital stay except for a slight elevation of temperature the fifth and sixth days due to an upper respiratory infection. The child was discharged on the ninth day as well. Diagnosis: Enterocolitis.

#### SUMMARY

1. Acute intussusception is the most common cause of obstruction in infancy.
2. History of acute intussusception is classical: Sudden acute pain in a healthy infant; early symptoms of shock with its

pallor, rapid pulse, sweaty skin, vomiting; abdominal mass; the finding of blood in the rectal examination is practically a criterion of this condition. Diagnosis can be further substantiated by x-rays in which the barium enema shows blockage along the bowel tract in the case of intussusception.

3. Early operation is advised since, if done early, the operation will consist merely of a manual disinvagination and carries a small risk. Operation done in cases after thirty-six to forty-eight hours are prone to require some form of resection with its attendant high mortality. These forms of resection are listed.

4. Palpation of an abdominal mass in acute intussusception is a late sign and should be considered in prognosis more than in the diagnosis.

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# MANAGEMENT OF THE BURNED PATIENT\*

DONALD C. GEIST, M.D.

Diplomate of the American Board of Surgery

PHILADELPHIA, PENNSYLVANIA

THE management of the burned patient constitutes an important surgical problem. Vital statistics reveal that there has been little reduction in the mortality in the United States from the year 1930 to 1938 inclusive. During the year 1939 a significant decrease in mortality did occur. Whether this reflects the effects of the renewed interest in the burn problem in the past few years is difficult to decide. McClure has called attention to these facts and has stressed the necessity for both the prevention of these injuries and their more thorough treatment. Cohen, in an article on the management of burns in the present war, has suggested the necessity for a "prepared routine of treatment" a thought which may be useful in civilian surgery.

An experience with the management of seventy burned patients in a general hospital leads to the belief that much emphasis must be placed on the treatment of the patient as a whole rather than stressing either the local or systemic manifestations. These cases can be divided into two equal groups, one being treated by the tannic acid method and the other by a variety of methods. Such a series is too small for detailed statistical deductions but certain facts stand out as deserving emphasis. (Table 1.) Seventeen or 24.2 per cent of these patients died and of these deaths 50 per cent had one-half or more of their body surface burned. The majority of the patients who died (76.5 per cent) were under ten or over sixty years of age. Seventy and five-tenth per cent of the cases had 25 per cent or more of body surface burned. The majority of the deaths (94.1 per cent) occurred within the first seventy-two hours, only one death coming after that period.

This fact held true regardless of the method of treatment employed, an observation noted by McClure, Glover and others. The mortality was greater in the tannic acid series (28.5 per cent) than in the other (20 per cent). However, in this group, there were twice the number of individuals with 50 per cent or more of their body surface burned, a great number at the extremes of age and a greater number of cases of initial shock. Hence, no great significance should

TABLE I  
STATISTICAL INFORMATION IN SEVENTY PATIENTS  
TREATED FOR BURNS

Total number of patients.....	70	Per Cent
Total mortality.....	17-24.2	
Mortality in tannic acid series.....	10-28.5	
Mortality in pretannic acid series.....	7-20	
Infection in tannic acid series.....	5-14.2	
Infection in pretannic acid series.....	9-25.7	
Percentage of deaths within twenty-four hours	10-58.8	
Percentage of deaths within forty-eight hours.	13-76.4	
Percentage of deaths within seventy-two hours	16-94.1	

be attributed to this difference in mortality. The incidence of infection was definitely lower in the tannic acid group, 14.2 per cent as compared to 25.7 per cent in the group treated otherwise.

A brief discussion of the various theories concerning the cause of death and altered physiology in the burned is necessary for the proper understanding of their care. In 1925, Davidson described the tannic acid method of treatment. He believed that the toxemic theory offered the best explanation of the sequence of events in this injury and that the production of a coagulum by the local application of tannic acid solutions prevented the absorption of toxic substances of some type from the burned tissues. Modifications of the method have been advocated since his work and of these

\* From the Surgical Service of Dr. J. A. Kelly, Misericordia Hospital, Philadelphia, Pennsylvania.

the combination of tannic acid and silver nitrate as described by Bettman seems to offer improvement. Bettman believes that

that hemoconcentration was caused by an increased capillary permeability with the escape of fluid into the subcutaneous tis-

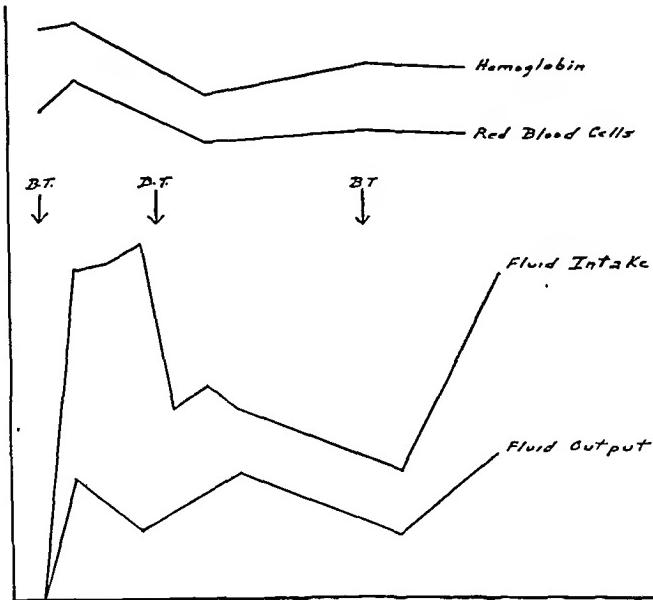


FIG. 1. Graph showing correction of hemoconcentration in a severely burned patient. Initial hemoglobin was 105 per cent and initial red cell count 5,350,000. B.T. signifies blood transfusion.

the almost immediate formation of a soft pliable eschar resulting from this combination has decided advantages over the slower method of tannic acid spray. Others have added antiseptics such as gentian violet, acriflavine or methyl violet to the tannic acid solution. Murless and Cohen have recently described their use in the treatment of burns occurring in the present war.

Underhill, Kapsinow, Fisk and Merle, in 1923, studied a series of twenty-one severely burned patients and found definite and marked evidence of concentration of the blood in the burned person. This hemoconcentration could readily be demonstrated by repeated hemoglobin determinations. The degree was proportionate to the extent and severity of the burn. They also showed that by forcing intake hemoconcentration disappeared and the patient improved. They believed that an increase of 40 per cent of the normal, if maintained for a considerable time, was incompatible with life. In 1930, Underhill and co-workers found in experiments on burned rabbits

tissues. They believed that the flow was in only one direction and that the fluid loss from the blood could reach as much as 70 per cent of the blood volume. Additional experiments led these observers to the opinion that this loss was plasma and that the edema fluid had a higher percentage of nonprotein nitrogen, potassium, manganese and inorganic phosphorus. They found, too, that the blood chlorides were decreased only in those cases which had extreme degrees of hemoconcentration. McIver, Black, Elkington and many others have demonstrated the presence of such homoconcentration.

It remained for Aldrich to propose another explanation. Aldrich cultured a group of burned patients from the onset of the injury through a large part of their course. He found that during the first twelve hours the burns were sterile but that after that time he was able to culture beta hemolytic and gamma streptococci in 100 per cent of the cases. Moreover, after forty-eight to fifty-six hours pure cultures of

these organisms could be secured. He believed, therefore, that such infection was the cause of these events. Aldrich then advocated the treatment of the burned with a 1 per cent aqueous solution of gentian violet as a spray until an eschar was produced. By the use of such therapy excellent results have been reported. Although there is no question as to the part played by infection late in the course of burns, it seems difficult to explain the early deaths by such a mechanism.

Further investigation of the hemoconcentration and fluid exchange in the burned patient shows that because of the increased capillary permeability and stasis there is a loss of plasma proteins with a decrease in plasma volume and total blood volume. Elkington, Russell, Wolff and Lee have demonstrated these changes and believe that the protein loss may be replaced by plasma transfusion with improvement of the patient. They call attention to the fact that the abnormal permeability persists for thirty-eight to forty hours and after this time the condition may be corrected by one large plasma transfusion. These workers have evolved a formula for the determination of the amount of plasma needed. Lucido, McClure, Black, Trusler and many others have called attention to the loss of plasma protein and the benefits of plasma or blood transfusions. According to many observers the simple forcing of fluids may not be sufficient to correct the hemoconcentration and may, by alteration in electrolytes, cause harm. Trusler has called attention to the similarity between such a situation and water intoxication. Many have stressed the necessity for plasma rather than blood transfusions claiming that whole blood may be injurious in the presence of marked degrees of hemoconcentration. We have no experience with plasma transfusion in the burned but are convinced that whole blood has saved many patients and has apparently not been harmful.

Evidence of liver damage in burned patients has been demonstrated by de-

creased values in liver function tests and in the postmortem changes found in the liver of those dying. Wolff, Elkington, Russell and Rhoades have investigated liver function tests in such patients and found definite evidence of lowered function by the bromsulphalein and hippuric acid liver function tests and prothrombinemia. In addition changes in the bilirubin and dextrose tolerance were suggestive of lowered hepatic function. Belt reported the autopsy findings in four patients dying of severe burns. He described two types of change in the liver: marked areas of mid-zonal necrosis and fatty degeneration throughout the liver. McClure states that degrees of liver necrosis thought to be incompatible with life were found in four of five such autopsies. Wilson, Macgregor and Stewart called attention also to the mid-zonal necrosis and fatty degeneration in their patients dying of acute toxemia of burns. Whether these findings are the result of a specific toxin, infection or anoxia is unknown.

The theory of a specific burn toxin is being revived. Wilson, Roxburgh and Stewart suggest such a toxin as the result of experiments in which they injected into rabbits the edema fluid from burned tissues. They were able to secure toxic effects either by subcutaneous, intravenous or intraperitoneal injection. When these animals were autopsied, the liver changes mentioned above were found.

Many of the changes described in the foregoing have been found in our patients. Sufficient studies were done on eight of these patients to show that a moderate or severe degree of hemoconcentration is often seen. The accompanying graph (Fig. 1) shows such change with its correction on the forcing of fluids and use of blood transfusion. Blood chlorides were determined on a group of these people and the values are listed in the accompanying table. (Table II.) They were decreased in two instances in one of which the patient died before a further check could be made. It is not known, therefore, as to whether the change

was significant. In the other the decrease was correct and disappeared on intravenous therapy. Serum proteins were done in three of these patients and showed a slight reduction of total protein in all of these. It was not marked. A shift of the albumin-globulin ratio with return to normal after blood transfusion occurred in one of these. The actual figures are given in Table III. Liver function tests have been done in one recent instance. This patient showed a definitely lowered hippuric acid liver function test and a dextrose tolerance curve suggesting lowered hepatic function.

TABLE II  
BLOOD CHLORIDES IN TEN BURNED PATIENTS

Patient	Adm. Date	Date of Test	Blood Chlorides	Per Cent of Body Surface Burned
D. R.	11/23/34	11/23/34	420	10
R. C.	2/16/36	2/17/36	430	25
W. R.	10/24/36	10/25/36	480	5
L. D.	11/16/36	11/17/36	464	50
		11/24/36	500	
S. B.	12/15/37	12/16/37	500	20
C. H.	12/16/37	12/17/37	460	10
M. F.	5/6/38	5/7/38	460	5
C. R.	10/23/39	10/24/39	428	55
		10/27/39	500	
		2/26/40	420	
		3/4/40	440	
		3/12/40	460	
F. R.	5/3/40	5/3/40	360	80
J. N.	11/17/40	11/18/40	340	15

Average normal for laboratory—450–500 mg. per 100 cc.  
Patient F. R. died before repetition was possible.  
Patient J. N. corrected by intravenous salt solution.

#### GENERAL OR SYSTEMIC TREATMENT

The first consideration is concerned with the care of shock. Adequate use of morphine or other sedatives to control pain is necessary. External heat must be used to restore body temperature. Fluid balance must be corrected and especial attention paid to adequate amounts of water, chlorides and proteins. The fluid intake of water must be sufficient, in some instances 4,000 to 6,000 cc. being necessary in every twenty-four hours. Bettman says 1,000 cc.

of fluids should be given every twenty-four hours for every twenty-five pounds of body weight. Chlorides are best given by intravenous salt solution and proteins supplied by repeated plasma or blood transfusions, frequently in large amounts. In the series of burns reported here we have used blood transfusion in large amounts in the first few days especially. The importance of such treatment especially in the first seventy-two hours after injury is attested to by the high mortality during this period. Reduction in mortality may be possible by more attention to this interval of time.

Chemotherapy has been suggested as a part of the treatment of burns. Cohen, in a report on a series of burns treated in the present war, stated that all were given sulfanilamide for the first five to six days because of the danger of infection. Wilson, Macgregor and Stewart believe that chemotherapy is a help although they state that the number of cases in which they used it was not great. Penberthy and Weller used sulfapyridine in six cases in their series, one of whom had a bronchopneumonia and two a septicemia. They advocate its use, especially in those who develop a complicating pneumonia. We have used sulfanilamide in two patients to hasten the decrease of infection and it improved each of these patients. Sulfapyridine was used in one of these but had no effect.

#### LOCAL TREATMENT

The tannic acid method or some modification such as the tannic acid-silver nitrate method has been most useful in local care. Glover, McClure, Penberthy, Mason, Beekman and many others have testified to the decrease in mortality since Davidson's introduction of this method. Almost all have agreed to the greater ease of use, shorter hospitalization and lessened pain achieved by it. In addition there is less scarring and decreased necessity for skin graft and other reconstructive measures. This has been true of the series reported here. In addition these cases strongly

support the lessened infection as mentioned earlier in the paper.

The technic for this procedure has been described many times. McClure and others have stressed the necessity for strict asepsis. The same technic must be used in

TABLE III  
SERUM PROTEIN IN THREE BURNED PATIENTS

Patient	Total Protein	Serum Albumin	Serum Globulin	Per Cent of Body Surface Burned
C. R.	5.7	3.6	2.1	55
	5	3	2	
	5.7	3.1	2.6	
	4.7	3.5	1.2	
	4.1	2.5	1.6	
	5.9	3.6	2.3	
(Last three values above found late in course of burn from large granulating surface, vomiting and refusal to eat. Correction by blood transfusion—high protein diet—vitamin B complex)				
J. N.	6	1	5	15
	5.7	3.1	2.6	
F. R.	6.3	4.3	2	80
	5.7	4.1	1.6	

Average normal for laboratory given as 6.7 mg. per 100 cc.

the dressing of the burns at their various stages. This means, of course, the use of sterile supplies, gloves, caps and masks. Following the careful cleansing, under anesthesia if necessary, the burned areas may be treated with tannic acid or one of its combinations. If the patient is admitted in shock, the procedure must wait the correction of it. When the eschar becomes loose it must be removed and the wound carefully débrided. The management of the granulating wound after removal of the eschar is a matter of preference. Our own group has been cared for with sterile vaseline gauze and dry dressings with the addition of 1 per cent gentian violet to infected areas. Glover and his associates have advocated early removal of the crusts and continuous use of Dakin's solution dressings to the granulating areas. Dakin's solution was used in some of the earlier cases of this series when they became

infected and quickly relieved the infection. A great many of the early cases in this group were treated by a variety of local applications of ointments, solutions and wet dressings. In reviewing them in comparison with the tannic acid group there is no doubt of the efficacy of the latter method. Frequent débridement of burned areas and the early use of skin grafting are very helpful.

#### LABORATORY INVESTIGATION

Routine laboratory studies aid in the management of burns. Daily urinalysis, frequent determination of hemoglobin, red cell count and hematocrit are necessities. Regular determinations of plasma proteins should be made especially in the early period. Blood urea nitrogen and nonprotein nitrogen values are an aid. Blood chlorides should be determined if indicated. Some type of liver function test should be done. Frequent leucocyte counts and cultures of the burned areas are necessary. Other determinations are done as indications arise. The frequency of such investigation depends upon the patient's progress.

#### CONCLUSIONS

A review of a small series of burned patients treated in a moderately sized general hospital is given. The various theories concerning burns and their treatment are briefly summarized. The necessity for some planned routine of treatment which considers the burned patient as a complete therapeutic problem is suggested and the essential elements of such a plan are outlined. The stressing of these facts should aid in the treatment of such patients in general hospitals to which most of them are admitted.

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ARGYRIA is characterized by a bluish- or slate-gray hue of the skin, due to deposits of silver salts in the tissues. In rheumatoid arthritis, patchy or diffuse areas of increased pigmentation not infrequently appear on the extremities or, less often, the face.

# THE TREATMENT OF TRAUMATIC AND WAR WOUNDS OF THE VASCULAR SYSTEM\*

GERALD H. PRATT, M.D.

Assistant Clinical Professor of Surgery, Post-Graduate Medical School, Columbia University  
NEW YORK, NEW YORK

EXPERIENCE in a large vascular clinic with an attendance of approximately 120 patients a week has

vessel is adequate and more satisfactory. While it seems unnecessary to stress the point, patients still bleed to death, even

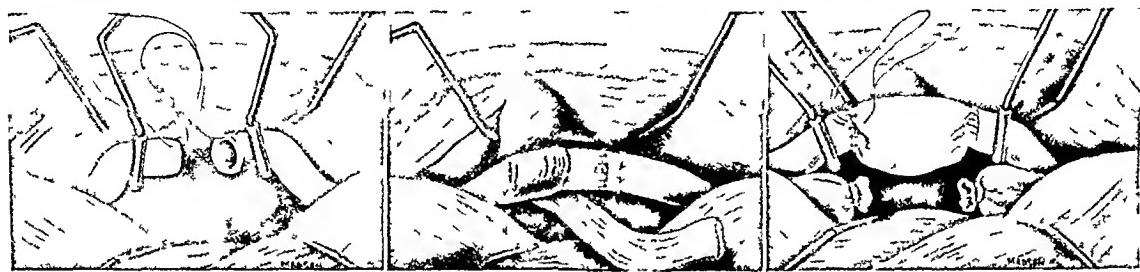


FIG. 1. A, end-to-end arterial suture; fine silk; needle does not enter intima. Elevation of artery from its bed and flexion of joint allows approximation. B, re-enforcement of suture line with nearby muscle or fascia. C, section of vein used to replace destroyed artery. When clamps are removed, vein wall shrinks to size of arterial blood column.

demonstrated how neglected has been the teaching in the management of the vascular problems and diseases. With our participation in a major and serious war, this knowledge of vascular problems becomes a necessity for the military surgeon. The decision as to amputation must be made by the operating surgeon and this decision may affect not only the limb but the life of the individual as well. Belated efforts to give this special training to the men called into the service necessarily will fail. Certain fundamental, underlying principles may be helpful.

While the tourniquet may be life saving, its incorrect application may prevent restoration of the circulation. The tourniquet, when used, should be applied as close to the wound as feasible; and where extra pressure is required for hemorrhage control, this should be a well padded object applied directly over the vessel just proximal to the laceration site. In many instances the application of a clamp to the bleeding

with medical attendance. Digital pressure is sufficient to stop hemorrhage and in relays it has been used over several days time. When a tourniquet has been applied, the operation should be performed at the nearest available hospital. Circulation has been restored, however, in closed vessels even after forty-eight hours.

## OPERATION

The surgeon must be taught that amputation, while sometimes necessary, should be performed as a last resort. Mere laceration of a major artery is not an indication for amputation. With the severance of an artery, an end-to-end arterial suture can be accomplished in many instances. The suture material should be fine and the needles minute. The needle should not enter the intima. Inasmuch as the pressure on the arterial wall at any point is inversely proportional to the rate of flow, very few sutures will be necessary. A muscle or fascial layer can be used to reinforce the

\* From the Surgical Vascular Clinic, New York Post-Graduate Hospital and Medical School, Columbia University.

suture line. (Fig. 1A and B.) When a section of artery has been lost, the defect up to 5 cm. can be closed by lifting the vessel from

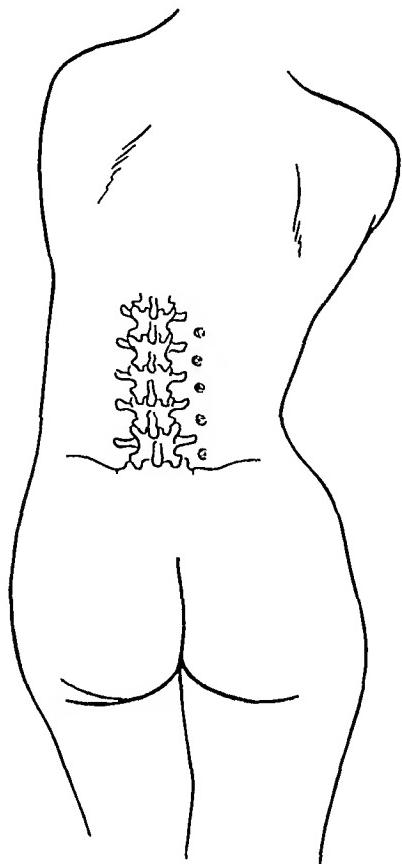


FIG. 2. Position of patient for perivertebral nerve block. Dots placed 4 cm. lateral and between the spines. Twelfth dorsal, first, second, third and fourth lumbar outlined.

its bed and flexing the limb. Venous transplants (Fig. 1C) to carry the arterial circulation have been successful in many instances. With the availability of heparin and dicoumarin\* this plastic arterial surgery has been modernized and is now routine in a vascular surgeon's practice.

Arterial thrombi, present in 50 per cent of injuries to arteries, should be removed prior to suturing. These can be lifted out with a forceps or the use of a silver wire corkscrew, as in the removal of emboli.

\* WRIGHT, I. S. The use of (dicoumarin) 3,3'-methylenebis-4 hydroxyoumarin in man—preliminary observation. (In press. *Bulletin, N.Y. Academy of Medicine*.)

When arterial ligation is necessary or has already been performed, the loss of the limb does not necessarily follow. The femoral ar-

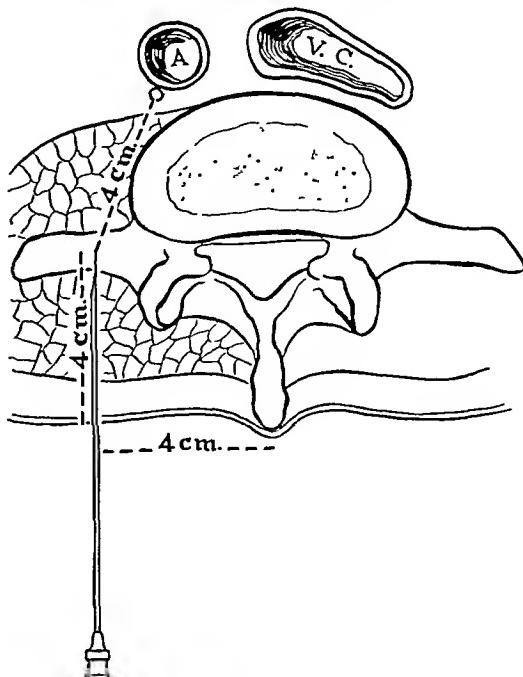


FIG. 3. Perivertebral nerve block lumbar area. The needle is introduced 4 cm. lateral to the intraspinous space, thus missing the transverse process. After introducing the needle 4 cm., its direction is slightly varied medially and advanced 4 cm. more. Careful aspiration eliminates intradural or intravenous injection.

tery may be ligated in 18 per cent without gangrene and this may be decreased to approximately 8 per cent by ligating the accompanying vein. The ability of the collateral circulation to take over the nutrition of a limb after the closure of a major vessel is stupendous, especially when stimulated.\* The physiological action of these collateral vessels, following a major vessel insult, is to go into spasm. This spasm probably prevents the development of thromboses. After the major vessel has been repaired or ligated, efforts to dilate and expand the collateral circulation should be taken. These are:

1. *External Heat.* This must be graded and is best maintained between 88° and 96°.

\* WRIGHT, I. S. Conservative treatment of occlusive vascular disease. *New England J. Med.*, November, 1941.

2. *Postural Changes.* Elevating the leg, leveling the leg and lowering the leg constitutes a mild vascular massage. With the oscillating bed this may be made continuous.

3. *Abstinence from Tobacco.* This is most important, as it seems routine to "stick a cigarette in a wounded soldier's mouth," whether he can breath or not. It has been proved without question that nicotine will cause small arterial vessels to go into spasm and if these small vessels are all that are carrying the patient's circulation, circulatory failure to the periphery will result. This cannot be overemphasized.

4. There are *certain drugs* which help reduce spasm and dilate collateral vessels. One of the best and most acceptable from the patient's standpoint, is alcohol in the form of whiskey. Deproteinated pancreatic tissue extract, an adrenalin neutralizing product, also aids in reducing vessel spasm. Such smooth muscle dilators as pantopon, papaverine and atropin, likewise may play a part.

5. The *part the sympathetic system plays* in the spasm of major and collateral vessels is now well understood. A perivertebral sympathetic nerve block, using novocaine, gives temporary sympathectomy effect and is most helpful in re-establishing circulation. The armamentarium is uncomplicated, the technic is simple and with training, any qualified surgeon can perform it safely. This should be a routine procedure in any major vessel injury. (Figs. 2 and 3.)

In some amputations, the refrigeration technic will have its place. Ice usually is available in all hospitals. The technic, as we have followed it, is to pack the limb to be amputated in ice to the groin. Thirty minutes after this packing, a tourniquet is applied and the limb replaced in the ice.

One and a half to two hours thereafter amputation can be performed painlessly and without shock. If the amputation is in the thigh, the sciatic nerve should be anesthetized with local anesthesia prior to its division.

While amputation technic is beyond the scope of this paper, it might be emphasized that morbidity and mortality can be minimized if certain points are followed: (1) Thoroughly cleanse the area to be amputated; (2) do not make muscle or fascial flaps; (3) close the wound with two or three sutures only; in doubtful cases, leave open; (4) immobilize the amputation stump and protect it from soiling; do not dress it for two weeks unless systemic reaction requires it; (5) use prophylactic gas gangrene, tetanus serum and sulfa drugs.

Discussion of the sulfa group of drugs has not been included in this paper because of the many articles already describing their use.

#### SUMMARY

Surgeons in general have not been trained in the management and treatment of the lesions involving the vascular system.

Knowledge of these lesions will become increasingly important with our participation in a major war.

It is not necessary to amputate when a major vessel has been severed.

Arteries may be repaired by suturing or venous transplants.

Many methods of stimulating collateral circulation are available.

Perivertebral sympathetic nerve block has proved helpful.

In neglected or advanced gangrene requiring amputation, the refrigeration technic reduces the mortality.



# LARGE BONE METASTASES FROM CARCINOMA OF THE BLADDER\*

CHARLES C. HERGER, M.D.

AND

HANS R. SAUER, M.D.

Diplomate of the American Board of Urology;  
Attending Urologist, New York State Institute  
for the Study of Malignant Diseases

Assistant Urologist, New York State Institute  
for the Study of Malignant Diseases

BUFFALO, NEW YORK

METASTASES from carcinoma of the bladder to the regional lymph-nodes and visceral organs are common especially in the late stages of the disease. Their incidence is placed by various authors at from 8 per cent (Bladder Tumor Registry of the American Urological Association) to 56 per cent (Leadbetter and Colston) of the cases with vesical cancer.

In many instances it is difficult for the clinician to demonstrate the presence of metastases, because the clinical manifestations often do not point to the organ or organs involved. Besides, these manifestations are frequently overshadowed by the severity of the symptoms produced by the primary lesion. Metastatic involvement of retroperitoneal lymph-nodes, liver, spleen and kidneys may be frequently suspected by the urologist, but an exact diagnosis can be made only if the size of the metastases permits their palpation, or if secondary clinical signs and symptoms develop. On the other hand it is fairly easy to demonstrate roentgenologically metastatic foci in the lungs or in the skeleton, while involvement of the superficial lymph-nodes can be diagnosed readily by palpation and biopsy.

It is obvious, therefore, that reliable data as to the incidence of metastatic lesions from carcinoma of the bladder can be obtained only from autopsy material. This statement is illustrated best by comparing statistics based on clinical observation with those based on postmortem examination. For instance, Judd reported

that but twenty-one or 12.6 per cent of 166 patients, who died of the disease, were known to have had metastases, while Leadbetter and Colston found metastases in fifty-five or 56.1 per cent of the cases in an analysis of ninety-eight autopsy cases. In the study of their material Leadbetter and Colston came to the conclusion that in fifty-one of their fifty-five patients death occurred from uremia and infection and not from general carcinosis.

Reports by various authors agree that metastatic involvement of the skeleton is common in all cases in which widespread metastases are encountered. However, cases with such large bony metastases that they dominate the clinical picture, are comparatively rare and they receive little or no attention in the various textbooks in urology or pathology. For instance, no case of carcinoma of the bladder producing bone metastases was found by Moore in a report based on sixty-five cases of metastatic bone lesions. In a study of 334 cases of skeletal metastases Geschickter and Copeland found but one case in whom the primary tumor originated in the bladder. Of 1,032 patients with metastatic bone lesions, collected by Sutherland, only nine were from bladder tumors. Only Graves and Militzer suggest that metastatic lesions to the skeleton occur more frequently than generally supposed. They found evidence of metastatic bone lesions in five patients or 11.6 per cent of forty-three consecutive cases of bladder carcinoma. It appears probable, however, that the figures presented by these authors are accidentally

\* From the State Institute for the Study of Malignant Diseases, Buffalo, New York, Burton T. Simpson, M.D., Director.

high, since the total number of forty-three cases is too small to permit conclusions as to the incidence of bone metastases from

Leadbetter the primary tumor was thought to have been controlled or even eradicated.

The part of the skeleton most frequently



FIG. 1. Case 1. A, osteolytic bone lesion from solid infiltrating carcinoma of the bladder; B, ten months later; further progression of lesion and pathological fracture of tibia.

bladder tumors. Statistics based on larger clinical material point to a less frequent occurrence. Herbst found an incidence of 2.2 per cent (139 clinical cases), Judd of 3.0 per cent (166 autopsy cases) and the Tumor Registry of the American Urological Association reported metastatic bone lesions in 3.7 per cent of 902 cases studied.

Bone metastases from carcinoma of the bladder are usually of the osteolytic type and only a few isolated reports (Kretschmer, Graves and Militzer and Livingston) indicate that attempts at new bone formation might occur in some instances. Once metastases to the bone have developed, they grow rapidly and may attain considerable size. For instance, in the case reported by Wells, a secondary tumor of 1640 Gm. was found at autopsy in the sternum.

Reports in the literature indicate that there exists no relationship between extensiveness of the primary lesion and tendency to formation of secondary bone lesions (Herbst). Case reports by Kretschmer, Burkland and Leadbetter give evidence that comparatively small primary carcinomas without much evidence of infiltration may be responsible for the development of extensive bone metastases. In some of the patients reported by Burkland and

involved by metastases is the pelvic girdle (Graves and Militzer). Of twenty-three cases with metastatic bone lesions which we collected from the literature,\* the secondary tumor was found in the pelvic bones in seventeen instances. Aside from the pelvic girdle there seems to be no particular predilection for any bone.

It has been the experience of various authors (Lowsley and Kirwin, Smith and Mintz, Herbst, etc.) that generalized carcinosis including multiple small-size foci to the bones is encountered more frequently in the group of solid infiltrating tumors of the bladder. However, it appears from reports in the literature that the large metastatic lesions to the skeleton are seen more frequently in tumors of the papillary type. Of the twenty-three patients already referred to before, sixteen had papillary cancers, the remaining seven had solid infiltrating carcinomas. The histological appearance of the tumor in the sixteen patients with papillary carcinomas was of comparatively low grade malignancy in some of the cases.

Large metastatic bone lesions were demonstrated in only four cases of 597 pa-

\* Burkland and Leadbetter, Graves and Militzer, Greenfield, Jonkinson, Livingston, Wells, Zeman.

tients with carcinoma of the bladder observed at the New York State Institute for the Study of Malignant Diseases during

anaplastic and extensive destruction of the bone structure was present.

Search for the primary lesion started with

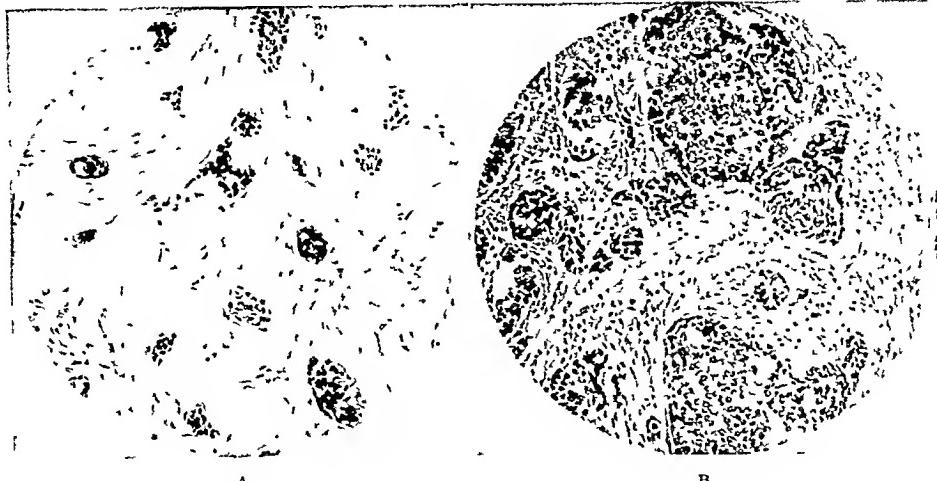


FIG. 2. Case 1. A, biopsy from bone lesion showing squamous cell carcinoma; B, biopsy from bladder tumor showing solid infiltrating squamous cell carcinoma invading bladder wall.

the past twelve years. It appears questionable, however, whether these four patients represent the total number of such lesions because many of our patients were not seen in their terminal stages, or were lost trace of shortly after admission.

#### CASE REPORTS

**CASE I.** F. A., No. 11930, sixty-eight years old, a white, male, was admitted to the hospital May 12, 1929. The patient gave a history of gradually increasing pain and lameness of his left leg beginning four months prior to admission. Examination of the left leg revealed swelling and tenderness over the middle third of the tibia extending over an area of 6 cm. in length. Otherwise the physical examination was essentially negative. The urine contained a trace of albumen and occasional white and red blood cells. The blood Wassermann was positive.

The x-ray picture of the left leg revealed osteolytic changes in the middle third of the tibia involving chiefly the cortex and the periosteum. (Fig. 1A.) Since a syphilitic lesion was suspected, antiluetic treatment was started which did not influence the condition. A biopsy from the lesion, made on July 6, 1929, proved it to be metastatic carcinoma. (Fig. 2A.) The tumor cells were partly squamous and partly

examination of the gastrointestinal tract which yielded negative results. Although the patient

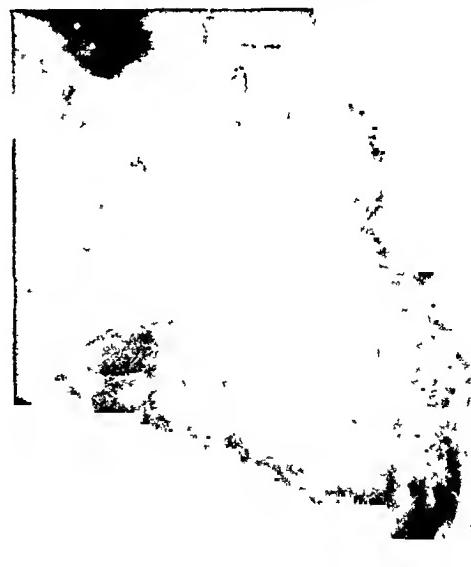


FIG. 3. Case II. Extensive bone destruction from papillary carcinoma of the bladder involving upper third of femur, acetabulum and inferior ramus of ischium.

had no symptoms referable to the genito-urinary tract, cystoscopic examination was

then performed which revealed a large, solid, infiltrating carcinoma originating in the left side of the trigone extending half way to the



FIG. 4. Case II. Biopsy from bladder tumor showing papillary carcinoma composed of regularly arranged, well differentiated squamous cells.

left lateral wall and to the vesical sphincter. Biopsy from the tumor of the bladder showed the same histology as the biopsy of the tumor obtained from the lesion in the left tibia. (Fig. 2B.) The tumor was a solid carcinoma of the squamous cell type with evidence of extensive invasion into the deeper layers of the bladder wall.

X-radiation over primary and secondary tumor as well as radon seed implantation into the bladder tumor had little influence on either. Repeated x-ray pictures of the left tibia revealed rapid progression of the bone destruction. An x-ray plate made on March 7, 1930, showed a pathologic fracture in the middle third of the tibia with extensive destruction of the shaft extending almost to the articular surface of the knee joint. (Fig. 1B.)

The patient died on May 28, 1930. An autopsy was performed and aside from the secondary tumor in the tibia, metastatic lesions of from 0.5 to 3.5 cm. in diameter were found distributed throughout both lungs.

The unusual feature of this case is the absence of signs and symptoms pointing to the presence of a fairly large primary carcinoma of the bladder although an extensive secondary tumor developed in the tibia. We believe that the secondary tumor growth in the tibia was embolic in origin, inasmuch as the autopsy findings revealed

extensive multiple metastases distributed throughout both lungs.

CASE II. S. M., No. 1837, forty-seven years



FIG. 5. Case III. Biopsy from bladder tumor showing papillary carcinoma invading the deeper layers of the bladder mucosa.

old, a white, male, was admitted to the hospital April 16, 1930. The patient gave a history of intermittent hematuria of ten years' duration. Six months prior to admission he complained of inability to walk due to gradually increasing pain and lameness in his left hip. On examination, swelling and tenderness of the left hip were found. This swelling extended well down into the soft parts of the thigh. The x-ray picture revealed an osteolytic lesion, evidently metastatic in nature, involving the inner side of the upper third of the femur extending into the femur neck and into the lesser trochanter. Foci of bone destruction were present also in the acetabulum and in the inferior ramus of the ischium. (Fig. 3.) No roentgenological evidence of lung metastases was found. On cystoscopic examination the bladder cavity was found to be filled with extensive infiltrating papillary tumors. Biopsy from the tumor of the bladder showed a papillary carcinoma of comparatively low grade malignancy composed of regularly arranged, well differentiated squamous cells. (Fig. 4.) Palliative 200 kilovolt x-radiation over the primary and secondary tumor had no effect and the patient died on August 28, 1930, four months after admission. No autopsy was performed.

This case proves the potential malignancy of comparatively low grade, malignant, papillary carcinomas of the bladder.

Although the primary tumor revealed little histological evidence of malignancy after having been present for more than ten

to be much more malignant than the primary tumor as evidenced by their rapid extension.



A



B

C

FIG. 6. Case III. A and B, one large and numerous small osteolytic areas in occiput due to metastatic involvement from papillary infiltrating carcinoma of the bladder; C, pathologic fracture of right humerus due to metastatic bone involvement.

years, metastases developed in the femur and ischium. It also is apparent that since such metastases have developed they prove

CASE III. W. K., No. 25033, sixty-two years old, a white, male, was admitted to the hospital May 15, 1936. The patient stated that he had

intermittent painless hematuria of four weeks' duration. Cystoscopic examination revealed a papillary carcinoma about 3 by 4 cm. in diameter.



FIG. 7. Case iv. Biopsy from bladder tumor showing papillary infiltrating carcinoma invading submucosa.

eter in the region of the left ureteral orifice. Biopsy from the tumor showed a papillary carcinoma with evidence of beginning infiltration into the deeper layers of the bladder mucosa. (Fig. 5.)

Treatment of the lesion consisted of 200 kilovolt x-radiation and transurethral resection followed by radon seed implantation. Cystoscopic examination on January 11, 1937, revealed an apparently healed bladder. The patient remained well until September, 1940, at which time a papillary recurrence 3 mm. in diameter was discovered at the border of the scar and it was destroyed by electro-coagulation. Two months later when the patient returned for re-examination no evidence of tumor growth was visualized on cystoscopic examination. However, he complained of pain in the region of the left occiput. Examination revealed an area of tenderness and swelling about 4 cm. in diameter in the left occipital region. X-ray plates of the skull showed an irregular somewhat rectangular area of bone destruction evidently of metastatic nature in the left occiput. Numerous punched out areas of from 0.5 to 1.0 cm. in diameter were also seen scattered throughout the entire occipital region. (Fig. 6A and B.)

The patient has not returned for re-examination since then but reports received from his

family physician indicated that he has been failing rapidly.

In April 1941, metastatic osteolytic lesions, involving medulla and cortex of the right humerus developed, and shortly after a pathologic fracture of the right humerus occurred. (Fig. 6c.)\* There also was enlargement and ulceration of the lymph-nodes in the right axilla. Later a general carcinosis with involvement of all lymph-nodes developed, although according to the latest report the patient was still alive in December 1941.

In Case III distant metastases from carcinoma of the bladder developed, although the treatment of the primary lesion seemed to be successful. In this patient no macroscopic evidence of the primary tumor was present at the time when metastatic bone involvement became apparent. It may be presumed in such cases that living tumor cells underneath the surface of the scar or bladder mucosa are responsible for the spread of the disease. A case reported by Leadbetter and Colston is of interest in this connection. Their patient developed a brain metastases although the bladder showed no macroscopic evidence of tumor on autopsy. However, on microscopic examination active tumor cells were found embedded in the scar and in the deeper layers of the wall of the bladder.

CASE IV. F. R., No. 42068, fifty-seven years old, a white, male, was admitted to the hospital June 4, 1941. The patient gave a history of intermittent painless hematuria of ten months' duration. During the past two weeks he complained of increasing pain in the left hip. Cystoscopic examination revealed multiple papillary infiltrating tumors of from  $1\frac{1}{2}$  to 5 cm. in diameter, the largest tumor being located high in the left posterior wall of the bladder. Biopsy showed that the tumor was a papillary carcinoma of the squamous cell type and some evidence of infiltration into the submucosa was noted. (Fig. 7.) A pelvic girdle plate, made on the day of admission (Fig. 8A) revealed no pathological condition in the left hip joint, however, an area of rarification of the bone structure in the lateral aspect of the

\* Figure 6c courtesy of Dr. John J. Brennen, Oswego, N. Y.

superior ramus of the pubic bone was noticeable. In spite of x-radiation, the patient complained of increasing pain in the left hip and

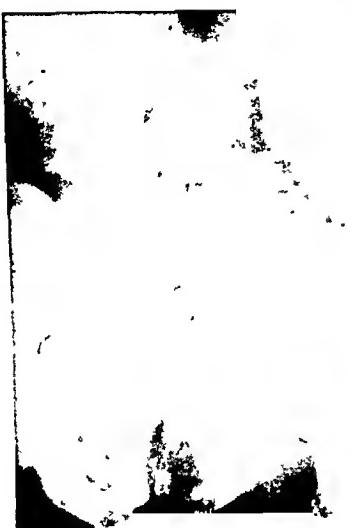
examination the entire left pelvic area was found to be infiltrated with a hard and nodular tumor mass. There was also marked edema



A



B



C



D

FIG. 8. Case IV. A, small area of rarefaction of lateral aspect of anterior ramus of pubic bone suggests early metastatic involvement; B, five weeks later; rapid progression of metastatic lesion; C, four months later; complete destruction of lower half of left pelvic girdle and invasion of tumor into head of femur; D, cystogram showing displacement of bladder to the right side by large tumor mass filling left pelvis.

an x-ray picture made five weeks later showed an osteolytic bone lesion involving the lateral part of the superior ramus of the pubic bone. (Fig. 8B.) The patient returned for re-examination on October 20, 1941. He had severe pain in the left hip and was unable to walk. On inspection a tumor mass was visualized filling the left lower quadrant and on bimanual

of the left leg. An x-ray picture of the left hip (Fig. 8c) revealed complete destruction of the superior and extensive destruction of the posterior ramus of the pubic bone. Marked involvement of acetabulum, ischium and ileum and invasion of the tumor into the femur head were also present. A cystogram showed the bladder to be displaced to the right side by a

large tumor mass filling the left pelvis. (Fig. 8D.) On cystoscopic examination marked progression of the lesion was found and since the patient's condition appeared hopeless no further treatment was given. He died January 6, 1942, seventh months after admission.

This case is of particular interest because it demonstrates the rapidity with which extension of metastatic bone involvement may take place once it has occurred. The metastatic lesion, which had affected only a small area in the anterior ramus of the pubic bone on admission, lead to almost complete destruction of the lower half of the left pelvis within four months.

The histological identity of the secondary bone lesion with the primary tumor of the bladder could be established only in the first of the four cases reported. In the remaining three patients the diagnosis was based on the roentgenological appearance of the bone changes and the symptoms produced by the secondary lesion. No evidence of a second primary carcinoma could be found in any of these three patients.

Severe pain in the affected parts of the skeleton was the outstanding symptom in all four patients and in Cases II and IV the pain was so severe that frequency of urination as well as marked dysuria were but secondary symptoms to the patient. The remaining two patients complained of little (Case I) or no bladder symptoms (Case III). Pathologic fractures occurred in two of the four patients while under observation (Cases I and III).

The primary tumor was of the solid infiltrating type only in one patient, while the remaining three patients had papillary carcinomas. This ratio is in agreement with the observation made before which was to the effect that large, destructive bone lesions seem to be encountered more frequently in the tumors of the papillary type than in solid carcinomas. If we add our four cases to the twenty-three collected from the literature, we arrive at twenty-seven patients, twenty of whom had papillary carcinomas as compared to seven who had solid infiltrating tumors. This observation is in

contrast to statistics dealing with the group of cases with generalized metastases. The development of generalized metastases is encountered more frequently in patients with solid infiltrating tumors, the ratio being about 2 to 1 (Smith and Mintz) in favor of the solid cancers.

Neither extent nor degree of infiltration of a bladder tumor represents an indication as to the likelihood of the development of metastatic lesions (Kretschmer, Greenfield, Burkland and Leadbetter). Two of our three patients with papillary carcinomas had tumors, the histological appearance of which suggested a low degree of malignancy, and one of them responded so favorably to treatment that the bladder appeared cystoscopically free of tumor at the time when the presence of the metastatic lesion became apparent. It can be concluded, therefore, that potentially active tumor cells may rest embedded in the scar or in the bladder mucosa even if it is believed that the tumor has been eradicated. These active cell rests may occasionally well be responsible for the formation of late metastases.

In all cases of carcinoma of the bladder the possibility of the development of bone metastases must be borne in mind. X-ray pictures should be taken if signs and symptoms develop which suggest the presence of metastatic bone involvement. Such metastases may occur also in tumors of low grade malignancy as well as in tumors which respond favorably to treatment.

#### SUMMARY

Metastatic involvement of the skeleton is common in all cases in which widespread metastases from carcinoma of the bladder are encountered. However, cases with large bony metastases which dominate the clinical picture are comparatively rare.

Four cases of large osteolytic bone metastases due to carcinoma of the bladder are presented. In one of these four cases the primary tumor responded so favorably to treatment that no cystoscopic evidence

of the tumor was present at the time when the secondary lesion became apparent.

Neither extent nor degree of malignancy of a bladder tumor represents a reliable indication as to the likelihood of the development of extensive metastatic lesions including bone involvement.

Three of the four cases presented had papillary carcinomas and only one case had a solid infiltrating cancer.

Study of the histology of the primary tumor in twenty-seven cases (twenty-three cases collected from the literature and the four cases presented) suggests that large osteolytic bone metastases seem to develop more frequently in cancers of the papillary type than in the group of solid infiltrating carcinomas. This observation is in contrast to the fact that general carcinosis is encountered more frequently in solid infiltrating cancers of the bladder.

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# ANOMALIES OF POSITION OF THE TRANSVERSE COLON

MAXWELL H. POPPEL, M.D. AND

Radiologist, New York University Clinic

SAMUEL T. HERSTONE, M.D.

Resident in Radiology, Montefiore Hospital

NEW YORK, NEW YORK

THIS paper will concern itself primarily with marked gross congenital abnormalities in position of the trans-

and withdrawal from the umbilical sac, rotation or descent; (3) fixation—bands, common mesenteries or variations in length



FIG. 1. A, Case 1: Common mesentery with elimination of the transverse colon. B, Case II: Normal transverse colon with common mesentery causing the greater portion of the ascending colon to lie below and parallel to the transverse colon. C, Case III: Common mesentery with nonrotation of the gut; left diaphragmatic herniation.

verse colon which may on occasion lead to serious clinical diagnostic errors. No attempt will be made to deal with apparent variations in position due to habitus, shape of abdominal cavity, paralysis or paresis of the diaphragm and abdominal musculature, or physiologic changes due to posture, respiration and digestion.

Anomalies of position in the digestive tract, just as anomalies elsewhere in the body, are the result of some failure in normal development. In the digestive tract where normal disposition of the gut within the abdominal cavity is a result of many complex movements, fixations and variations in growth, it is not surprising that many bizarre and unusual abnormalities in position occur.

Anomalies may result from: (1) Abnormalities in growth—shortening or lengthening, resulting in redundancies; (2) abnormalities in migration—movement into

of mesenteries; and (4) associated congenital abnormality of neighboring organs, e.g., the diaphragm.

These disturbances in normal development may occur singly or in various combinations. Not uncommonly all four may be present in a single case. In such cases it may be difficult to distinguish between cause and effect. For example, occasionally the question arises whether a band or common mesentery is responsible for a defect in rotation or vice versa. Very often this question cannot be answered.

Abnormalities of growth have been discussed at great length by Bryant, Kantor and others. The distinction between the normal and the abnormal is sometimes at best arbitrary. These defects will, therefore, not be discussed in this paper except as they occur in association with other abnormalities in development.

For purposes of simplicity, the clinically important anomalies of position of the transverse colon have been classified into four main groups:

lie in the midline almost parallel to each other, both having a common mesentery, with elimination of the transverse colon. (Fig. 1A.)

CASE II. In this case the cecum and



FIG. 2. A, Case IV.



FIG. 2. B and C, Cases V and VI: Examples of interposition of the transverse colon by the liver and diaphragm.

*I. Common Mesentery:* This anomaly is primarily one of fixation, but is often found in combination with abnormalities in rotation and diaphragmatic herniation.

CASE I. In this case normal rotation and descent have apparently taken place. The cecum is in the right lower quadrant, but the ascending and descending colon have come to

appendix are found to be in the left lower quadrant. It would seem that rotation and development have taken place normally, since the hepatic flexure is in the right upper quadrant. However, something has held the cecum in the left lower quadrant, resulting in an ascending and transverse colon lying parallel to and alongside each other. In this case the position of the transverse colon is

normal. This case is included in this series because of its allied interest. (Fig. 1B.)

CASE III. This is the most extreme case of

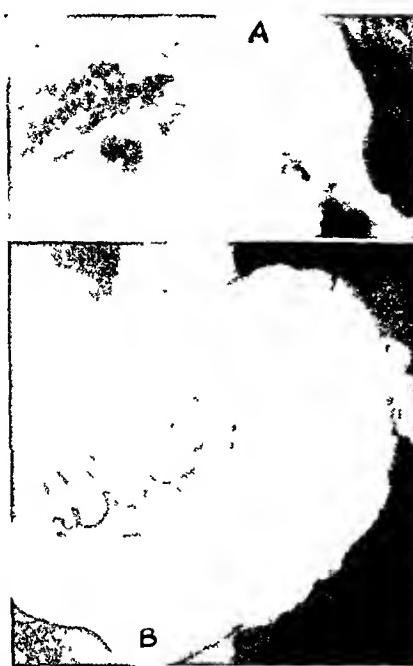


FIG. 3. A, Case VII: Bilateral interposition of the transverse colon. B, Case VIII: Interposition between the liver and anterior abdominal wall on the right and between the stomach and anterior abdominal wall on the left.

common mesentery. Here it is associated with nonrotation of the gut and left diaphragmatic herniation. The transverse colon is completely absent; the large intestine takes the shape of a hairpin, with but a single flexure lying high within the left chest. (Fig. 1C.)

*II. Interposition (Exclusive of Retroposition).* This group of anomalies is not nearly so extreme as are those of common mesentery. Interposition of the transverse colon between diaphragm and adjacent structures may be congenital or may be secondary to paralysis of the diaphragm and ptosis of the liver. This paper is primarily concerned with those cases in which ptosis of the liver and paralysis of the diaphragm are not present. Even after these have been ruled out, it may not always be possible to say that the interposition is due to a developmental defect. However, since it is an abnormality which

is not too uncommon, and one which occasionally results in serious diagnostic errors, it is worthy of consideration.

(a) *Left-sided Interposition.* Interposition of the colon between stomach and diaphragm and spleen and diaphragm is extremely common and one with which all radiologists are familiar. Undoubtedly, every radiologist has encountered difficulties in the study of the cardiac end of the stomach as a result of this abnormality.

(b) *Right-sided Interposition.* Interposition of the transverse colon between liver and diaphragm is much more unusual than left-sided interposition. This condition is of clinical importance, since on occasion it has led to an erroneous clinical diagnosis of diaphragmatic herniation. Cases IV, V and VI (Fig. 2A, B, and C), respectively, demonstrate this type of abnormality. Case V shows several diverticula near the hepatic flexure.

(c) *Bilateral Interposition.* This is a rare condition and is demonstrated in Cases VII and VIII.

CASE VII. In this case the colon is running along the undersurface of the diaphragm from the right upper quadrant to the left upper quadrant. (Fig. 3A.)

CASE VIII. This is a case of interposition between the liver and the anterior abdominal wall on the right, and the stomach and anterior abdominal wall on the left. This was confirmed in the oblique and lateral views. The colon is also shortened and has a slight upward arch. (Fig. 3B.)

*III. Herniae of the Transverse Colon.* These abnormalities usually occur as a result of persistence of the right or left pleuroperitoneal canals. Very rarely one sees complete absence of the diaphragm with most of the abdominal viscera in the chest. This, however, is incompatible with life and is of little concern to the radiologist.

(a) *Left-sided Hernia.* CASE IX. Most of the colon is in the left chest. There is partial arrest of rotation. The cecum and appendix are in the region in which the left diaphragm normally should be. (Fig. 4A and B.)

**CASE X.** In this case rotation is normal. The splenic flexure is in the left chest, drawing the distal transverse colon upward. (Fig. 4c.)



FIG. 4. A and B, Case ix: Most of the colon in the left chest; cecum and appendix are in the region in which the left diaphragm normally should be.



FIG. 4. C, Case x: Normal rotation; splenic flexure in left chest, drawing distal transverse colon upward.

**CASE XI.** This case demonstrates a diaphragmatic hernia associated with common mesentery and nonrotation. (Fig. 4d.)

(b) *Right-sided Hernia.* These are much rarer than those on the left side, but do occur.

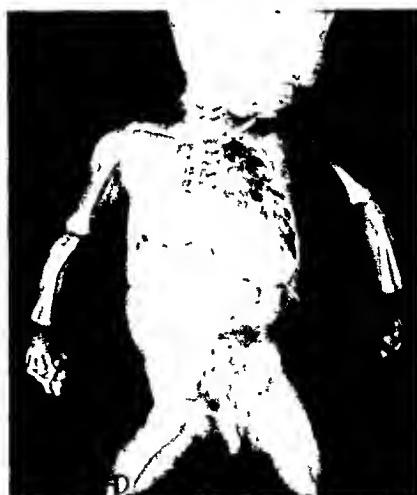


FIG. 4. D, Case xi: Diaphragmatic hernia associated with common mesentery and nonrotation.

(c) *Bilateral Hernia.* **CASE XII.** This is an extremely rare condition in which the ascending colon was seen to go through an opening in the right side of the diaphragm. The transverse colon then crossed from right to left within the chest and descended through an opening in

the left side of the diaphragm. It is hard to conceive how it could have developed embryologically, unless the transverse colon, or

xiii is a right oblique roentgenogram showing the transverse colon as it passes posterior to the stomach.



FIG. 5. Case XII: Transverse colon in relation to the inferior and right borders of the heart; bilateral hernia.

what corresponded to it, entered the chest before formation of the diaphragm. The diaphragm then developed around it. (Fig. 5.)

*IV. Retroposition.* This condition is also exceedingly rare. Only a few cases are reported in the literature—thirteen, according to Truesdale. It is due to a rotation of the gut in a clockwise rather than a counterclockwise direction, resulting in a posterior position of the transverse colon in relationship to the stomach, duodenum and remaining small intestines. Figure 6 in Case



FIG. 6. Case XIII: Right oblique roentgenogram showing retroposition of the transverse colon.

#### CONCLUSION

This paper has concerned itself primarily with an illustrated description of the marked gross congenital positional anomalies of the transverse colon.

Thanks are due to Dr. Charles Gottlieb for the use of Cases III and XII.

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# CLINICAL STUDIES OF LIVER FUNCTION\*

## I. THE EFFECT OF ANESTHESIA AND CERTAIN SURGICAL PROCEDURES

C. R. SCHMIDT, M.D.

Director of Research, Hertzler Clinic

R. T. UNRUH, M.D.

Resident Surgeon, Hertzler Clinic

AND

V. E. CHESKY, M.D.

Associate Surgeon, Hertzler Clinic

HALSTEAD, KANSAS

WITHIN the past decade the functional state of the liver has become a consideration of more than passing clinical interest in surgical patients lacking evidence of biliary tract or hepatic disease. It is becoming more and more apparent that the liver, a relatively "silent" organ with a tremendous functional reserve and regenerative ability, can be markedly deficient in this assumed factor of safety. More significant, increasing recognition is being given the fact that certain patients apparently normal in all respects possess a liver that can withstand ordinary living but, when an added burden is placed on this organ, the reserves prove distressingly limited. Clinical evidence of hepatic insufficiency frequently becomes manifest after operations on the biliary tract and following surgery on toxic goiters; but, as Boyce has emphasized repeatedly, subnormal hepatic function following operation is by no means confined to this group of surgical patients.<sup>3,5</sup>

During the past two years we have studied over 600 medical and surgical patients with several tests of liver function run serially. Our observations have confirmed in nearly all respects those reported by Boyce<sup>2,3,4</sup> which make this worker's studies more significant. Much of his material has been obtained on charity patients, many of whom were colored and whose diet and living conditions may be assumed substandard. The subjects we have studied were all private cases from a somewhat

higher social stratum, nevertheless, unexpected hepatic insufficiency was encountered in a surprisingly high number. We have satisfied ourselves that the liver plays an extremely important rôle in influencing postoperative morbidity and are in full accord with Boyce's concept of the "liver weakling"—an apparently normal individual with limited hepatic reserve who withstands a serious illness or an elective surgical procedure poorly, frequently developing clinical evidence of deficient hepatic function.

Studies of the functional state of the liver in goiter patients, before and after surgery, have been reported by us elsewhere.<sup>7</sup> Sixty per cent of 200 consecutive, unselected patients admitted to the goiter service revealed evidence of subnormal liver function. This figure is without regard for the type of goiter present or the age of the patient. Greatest impairment of liver function was observed in diffuse toxic hyperplastic goiter and in goiters of long standing with essentially normal basal metabolic rate (chronic hyperthyroidism). Specific therapeutic measures directed at a damaged liver were more effective in improving liver function when combined with the usual preoperative measures than when only the measures now in general use were employed alone.<sup>7,10</sup> A correlation between the functional state of the liver postoperatively and morbidity was observed.

This report concerns the effect of certain anesthetics and operative procedures on

\* From the Hertzler Clinic and the Surgical Service of the Sisters of St. Joseph Hospital, Halstead, Kansas.

liver function as measured by the hippuric acid test. We believe this test, which measures both the ability of the liver to synthesize and to conjugate, is concerned with an extremely important hepatic function, i.e., the function of detoxication. Benzoic acid, itself nontoxic in the dose administered in the hippuric acid test, is handled by the liver like a toxic substance. It is conjugated with glycine to form hippuric acid which is excreted in the urine. Impaired ability of the liver to detoxify and postoperative morbidity are closely related. Patients with subnormal liver function after operation have been observed to display a stormier postoperative course than subjects who have no difficulty in synthesizing hippuric acid from sodium benzoate. While it is impossible to predict on the basis of preoperative liver function the degree of impairment that an anesthetic and operative procedure will induce, it has been observed repeatedly that patients with subnormal liver function before operation prove poorer risks than patients without evidence of functional hepatic insufficiency.

We have made a comparative study of liver function in patients using the hippuric acid test, the bromsulfalein dye excretion test, prothrombin time, and blood amylase determinations.<sup>12</sup> Positive results by all of the tests were obtained in patients presenting clinical evidence of hepatic insufficiency; however, the hippuric acid test and prothrombin determinations made serially have proved the most satisfactory index of hepatic function in border-line cases, as well as in certain definitely poor risk patients who showed subnormal hippuric acid synthesis and diminished prothrombin values with both normal dye elimination and blood amylase values. This is not surprising when one considers the number and variety of hepatic functions. Of the various tests available we believe that the hippuric acid test run serially is most suited as a laboratory aid in helping to evaluate a patient as a surgical risk. At the same time, we agree wholeheartedly with Boyce that no test or

group of tests can be substituted for surgical judgment and clinical wisdom. While a "normal" hippuric acid test is in no way any guarantee of a patient as an operative risk, persistently subnormal values by the test are a warning of questionable hepatic reserve in the event such a patient is to be subjected to the added load of surgical trauma and an anesthetic. Such patients can be made better surgical risks by specific measures aimed at improving the functional state of the liver.<sup>5,10</sup>

Considerable animal experimentation has established the fact that the volatile (inhalation) anesthetics readily damage the liver. Chloroform is the most hepatotoxic with ether, ethylene and nitrous oxide next in order. It has been shown repeatedly that a liver rich in glycogen withstands anesthesia better than one depleted of glycogen. Also administration of oxygen along with the anesthetic likewise decreases liver damage.

Comparatively few studies have been reported on patients subjected to anesthesia and surgery in whom tests of liver function were performed both before and after the operation. Cantarow, Gartman and Ricchiuti<sup>6</sup> studied sixty patients subjected to simple cholecystectomy utilizing serum bilirubin and retention of bromsulfalein as a measure of hepatic function. They were unable to correlate the type or duration of anesthesia with postoperative drop in liver function following nitrous oxide and ether, infiltration of procaine hydrochloride, and spinal anesthesia type not specified. In twenty-six of forty-one patients (63 per cent) with apparently normal preoperative hepatic function a temporary increase in serum bilirubin was observed; retention of dye after operation was observed in 39 per cent of this group. Coleman<sup>8</sup> studied hepatic function in 100 patients subjected to surgery under various anesthetics. Retention of bromsulfalein and blood bilirubin in some were used as an index of hepatic function. Of thirteen patients receiving avertin 77 per cent showed retention of dye on the first day after

operation and 16 per cent still showed evidence of hepatic dysfunction on the seventh postoperative day. Of forty-nine patients operated upon under nitrous oxide-oxygen-ether anesthesia 51 per cent were unable to remove the dye in the allotted time one day after operation; by the seventh postoperative day 4 per cent still showed impaired dye clearance. Of eight patients subjected to spinal anesthesia 50 per cent showed evidence of functional liver damage on the day after operation; all had normal function on the seventh postoperative day. Thirty three per cent of twenty-seven patients operated upon under nitrous oxide-oxygen, and one patient operated upon under ether showed bromsulfalein retention on the first day, and two patients subjected to local anesthesia revealed no evidence of hepatic dysfunction. Boyce,<sup>3</sup> using the Quick hippuric acid test, studied an unspecified number of presumably normal patients subjected to elective surgery. Liver function was estimated before operation and on the first, second, third, seventh and fourteenth days postoperatively. Spinal anesthesia produced a drop of 49 per cent. Following ether a drop of 25 per cent was observed, while ethylene reduced hepatic function by 21 per cent.

#### EXPERIMENTAL DATA

All patients in this series were considered good operative risks and, except for patients undergoing cholecystectomy, were given no special preparation to improve liver function prior to operation. The hippuric acid test was performed usually on the day before operation and again on the first or second and the eighth days postoperatively. In a number of instances in which no drop in function was observed immediately after surgery the test on the eighth day was omitted.

*Spinal Anesthesia.* Spinal anesthesia was induced by the intradural introduction of crystalline novocain dissolved in spinal fluid. Two cc. of spinal fluid were with-

drawn and from 1½ to 2 cc. containing from 150 to 200 mg. of novocain were re-introduced. An intramuscular injection of ephedrine in dosage of 50 to 75 mg. was always administered prior to the intraspinal injection. Blood pressure determinations and pulse rate were taken by an assistant routinely at frequent intervals throughout the operation.

Table I shows the effects obtained on twenty-one patients between the ages of nineteen and seventy-one years subjected to a variety of surgical procedures under spinal anesthesia. In eighteen (85 per cent) the first postoperative test showed essentially no reduction or the decline was such that liver function still remained within the lower limits considered normal (4.5 Gm. or 90 per cent). In a few instances, so designated in Table I, the hippuric acid test was delayed until the second day after operation because the test solution produced nausea and could not be retained. Use of the intravenous modification of the hippuric acid test<sup>9</sup> was not done because on comparing values obtained by the oral and intravenous technics, run on consecutive days in twenty subjects having normal values with the oral method, we were unable to establish a satisfactory correlation which would justify such a substitution in a study of this sort.

It is interesting, and perhaps significant, that in two of the three patients showing a postoperative drop in liver function a marked transient fall in blood pressure occurred during the operation. In both adrenalin subcutaneously promptly elevated the blood pressure to its former level where it was maintained. It is possible that a state of temporary anoxemia secondary to a fall of blood pressure to shock levels, though only transient, could produce some degree of liver damage. Since no determinations of arterial oxygen saturation were made during the period of hypotension such an explanation is purely speculative. The reason for the drop in liver function from 85 to 62 per cent in the patient No. 21, age seventy-one, is unknown. The post-

operative period was not stormy and recovery was uneventful.

*Ether.* Ether anesthesia, administered

three minutes. It is not unlikely that the magnitude of such an extensive operative procedure as bilateral radical mastectomy

TABLE I  
EFFECT OF SPINAL ANESTHESIA AND SURGERY ON LIVER FUNCTION

No.	Sex	Age	Hippuric Acid Test* Four-hour Output (Gm.)*		Operation
			Pre-operative	Postoperative	
1	F	45	4.86	4.78 <sup>1</sup>	Perineorrhaphy, uterine suspension
2	M	19	3.80	3.76 <sup>1</sup>	Herniplasty; pituitary dystrophy
3	F	59	4.38	4.22 <sup>1</sup>	Uterine fixation
4	F	59	5.21	4.77 <sup>1</sup>	Cauterius, laparotomy
5	F	53	6.10	5.68 <sup>2</sup>	Gallstones; cholecystectomy
6	F	51	4.64	4.52 <sup>2</sup>	Gallstones; cholecystectomy
7	F	50	5.09	4.86 <sup>1</sup>	Gallstones; cholecystectomy
8	M	42	5.92	5.18 <sup>1</sup>	Gallstones; cholecystectomy
9	F	59	4.96	4.56 <sup>1</sup>	Hysterectomy
10	F	51	6.88	6.14 <sup>1</sup>	Perineorrhaphy, uterine fixation
11	F	48	4.59	4.48 <sup>2</sup>	Fibroids, hemorrhage; hysterectomy
12	F	33	4.74	4.47 <sup>1</sup>	Perineorrhaphy, uterine suspension
13	F	37	5.53	5.93 <sup>2</sup>	Defundation
14	F	71	4.54	4.68 <sup>2</sup>	Dilatation and curettage cancer of cervix
15	F	30	5.60	5.54 <sup>1</sup>	Endometrioma, excision
16	F	63	5.23	4.93 <sup>2</sup>	Perineorrhaphy, uterine fixation
17	F	58	4.72	4.95 <sup>2</sup>	Dilatation and curettage
18	F	46	5.38	4.50 <sup>1</sup>	Amputation leg
19	F	57	6.70	†3.73 <sup>1</sup>	†Uterine fixation; saphenous ligation
20	F	55	6.47	†2.43 <sup>2</sup>	Gallstones; cholecystectomy
21	F	71	4.26	3.14 <sup>1</sup>	Vaginal hysterectomy
Average.....			5.23	4.83 <sup>§</sup>	4.90

\* Average output one hundred fifty "normal" patients 5.0 Gm. in four hours following ingestion of 6 Gm. sodium benzoate; 4.5 Gm. considered lowest limits of normal.

† Fall in blood pressure during operation.

‡ Hippuric acid test 6.08 Gm. on twelfth postoperative day. Small numerals in postoperative columns designate day of test.

§ Excluding No. 19 and 20.

by the open drop method to sixteen female patients between the ages of twenty-three and sixty-three years decreased liver function by 11 to 60 per cent with an average of 33 per cent (Table II). Three patients (Nos. 29, 30 and 33) with initial liver function tests of 108, 96 and 100 per cent gave values of 44, 50 and 44 per cent, respectively, on the day following surgery. Subject No. 29 was a sixty-three year old lady with carcinoma in both breasts. Bilateral radical mastectomy was performed with a surgeon working on each side simultaneously. Ether was administered from forty-

was a factor in the observed 60 per cent drop in liver function. The other two patients were in their early twenties; in one (No. 30) ether was administered for an hour and fifty-four minutes, in the other (No. 33) for thirty-eight minutes.

While the ether series is too small to warrant sweeping conclusions, there is a rough correlation between duration of anesthesia and drop in liver function (Nos. 30, 32 and 35). Likewise, the majority of those patients whose abdomens were opened (Nos. 32, 33, 34 and 37) tended to exhibit lower liver function after operation

than the patients undergoing mastectomy, hemorrhoidectomy and nephropexy. In all of these patients liver function was within

of impaired removal of bromsulfalein by normal livers in dogs but that animals with dye retention evidenced even greater reten-

TABLE II  
EFFECT OF ETHER ANESTHESIA ON LIVER FUNCTION

No.	Age	Hippuric Acid Output in Four Hours—Gm.*			Per Cent Change	Operation	Duration of Anes- thic, Minute		
		Preoper- ative	Postoperative						
			1	2	3				
22	36	5.20	3.90 <sup>1</sup>	5.36 <sup>8</sup>	.....	-25	Excision of breast tumor		
23	53	5.10	3.80 <sup>2</sup>	4.22 <sup>7</sup>	5.60 <sup>17</sup>	-26	Radical mastectomy		
24	48	4.29	3.74 <sup>1</sup>	4.50 <sup>8</sup>	.....	-13	Radical mastectomy		
25	61	6.09	3.57 <sup>1</sup>	6.29 <sup>8</sup>	.....	-41	Radical mastectomy		
26	33	....	4.41 <sup>2</sup>	5.31 <sup>5</sup>	5.52 <sup>7</sup>	-20†	Radical mastectomy		
27	41	5.00	3.33 <sup>1</sup>	4.90 <sup>8</sup>	.....	-33	Radical mastectomy		
28	54	....	3.94 <sup>2</sup>	4.41 <sup>8</sup>	.....	-11†	Radical mastectomy		
29	63	5.40	2.21 <sup>1</sup>	5.31 <sup>7</sup>	.....	-60	Bilateral radical mastectomy		
30	23	4.84	2.51 <sup>1</sup>	5.58 <sup>10</sup>	.....	-48	Plastic on breasts		
31	46	4.80	3.97 <sup>2</sup>	4.39 <sup>5</sup>	.....	-17	Hemorrhoidectomy		
32	44	5.80	3.57 <sup>1</sup>	5.71 <sup>8</sup>	.....	-38	Perineorrhaphy, uterine fixation		
33	24	4.98	2.21 <sup>1</sup>	5.16 <sup>7</sup>	.....	-55	Perineorrhaphy, uterine fixation		
34	31	5.18	3.28 <sup>1</sup>	5.40 <sup>8</sup>	.....	-37	Bilateral salpingectomy, fixation		
35	42	5.60	3.55 <sup>2</sup>	5.20 <sup>8</sup>	.....	-37	Vaginal hysterectomy		
36	51	4.54	3.88 <sup>1</sup>	4.98 <sup>8</sup>	.....	-14	Nephropexy		
37	50	4.14	2.16 <sup>1</sup>	.....	.....	-48	Cholecystectomy		
Average...		5.07	3.38	5.10	.....	-33			

\* Normal = 5.0 Gm.; 4.5 Gm. considered lower limits of normal. Small numerals in postoperative columns designate day of test.

† Difference between column 1 and 2 or 3.

the range of normal before surgery. A drop of liver function to 40 to 60 per cent of normal was invariably attended by increased morbidity during the first few days following operation, after which uneventful recovery was the rule. One wonders, however, what the outcome would be if a patient with a significantly subnormal liver function, say 50 or 60 per cent of normal, were subjected to a major operation under ether. We have some information on this point concerning poor risk patients operated upon under spinal anesthesia.<sup>11</sup>

*Avertin.* Avertin ordinarily is used as a basal analgesia in combination with one of the volatile anesthetics, most commonly ethylene. Bourne and Raginsky observed that avertin produced little or no evidence

tion, indicating increased liver damage after avertin.<sup>1</sup>

We have studied liver function in seven patients before and after a surgical procedure under avertin narcosis. (Table III.) Thyroidectomy was done in six of the seven patients receiving avertin as a basal anesthetic (80 to 90 mg. per kilo body weight administered rectally). In addition to the avertin the thyroid region of the goiter patients was infiltrated with two ounces of 0.5 per cent novocain. The remaining patient had a carcinoma of the jaw and avertin was the only medication given. A drop in liver function of 5 to 30 per cent was observed on the second postoperative day. Two of the six patients with goiter presented clinical evidence of a quite toxic

goiter (Nos. 43 and 44). Liver function dropped 25 and 30 per cent, respectively, following operation. Patient No. 44 had a

our observation during the past two years; and this in spite of therapeutic measures to bolster liver function during the first two

TABLE III  
EFFECT OF AVERTIN ON LIVER FUNCTION  
(80 to 90 mg. per kilo body weight)

No.	Sex	Age	Hippuric Acid Output in Four Hours		Per Cent Change	Diagnosis and Operation
			Pre-operative	Post-operative*		
38	M	46	4.05	3.00	-26	Carcinoma jaw, excision and cauterization
39	M	40	5.20	4.97	-5	Nodular colloid goiter, thyroidectomy
40	F	44	6.00	5.29	-12	Nodular colloid goiter, thyroidectomy
41	F	41	5.89	5.23	-11	Fetal adenoma, right; lobectomy
42	F	29	4.76	4.00	-19	Nodular goiter; thyroidectomy
43	F	36	5.91	4.39	-25	Recurrent goiter; thyroidectomy
44	F	25	4.73	3.31	-30	Toxic diffuse goiter; hemithyroidectomy
Average.....			5.22	4.31	-17	

\* Tests made on second postoperative day.

diffuse hyperplastic goiter and required special preparation to raise the hippuric acid test to the normal range before operation. Only because of an idiosyncrasy to both morphine and the barbiturates was

days after operation. Although the first three postoperative days were stormy, the patient was never in critical danger.

Boyce<sup>3</sup> has found that ethylene anesthesia diminished liver function by an

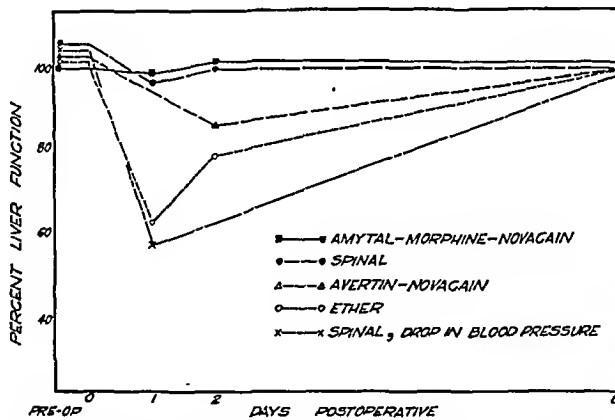


FIG. 1. Effects of anesthesia and surgery on liver function by the hippuric acid test in surgical patients. Compiled from data on forty-four patients tabulated in Tables I, II and III, and on forty patients operated upon under amytal-morphine-novocain anesthesia.

avertin used in this patient. The surgical procedure was restricted to hemithyroidectomy, yet postoperative liver function was diminished more than in any other well prepared hemithyroidectomized patient under

average of 21 per cent in apparently normal subjects undergoing elective surgery. It seems reasonable that the depressing effects of avertin plus ethylene would be cumulative. Theoretically at least, this would add

up to a 50 per cent decrease in liver function, a sizeable load to put on a patient with a very toxic goiter. A study of the effect of avertin plus ethylene anesthesia on liver function in toxic goiter should be made.

*Local Anesthesia.* Local anesthesia is still used widely in this clinic for surgical procedures other than thyroidectomy. We have accumulated data on the effect of surgical procedures under local anesthesia on liver function in over forty patients. Predominant in this group are nontoxic goiters, hernioplasties, skin grafts, neck tumors and cysts and benign tumors of the breast. Unless the patients are very young or very old the preoperative sedation is the same for all: 6 gr. of amyral and  $\frac{1}{6}$  gr. (H) of morphine sulfate two hours before and  $\frac{1}{6}$  gr. (H) of morphine one hour before surgery. The effect on liver function of this sedation together with from one to three ounces of  $\frac{1}{2}$  per cent novocain infiltration has been so consistently negative that we consider it pointless to tabulate the data. (Fig. 1.)

#### COMMENT

We have confirmed so many of Boyce's observations on liver function in surgical patients that we are at a loss to understand the conflict between his results on spinal anesthesia and those obtained by us. Boyce<sup>5</sup> recognizes that a blood pressure drop may have been a factor in the liver insufficiency he observed after spinal anesthetics, yet no data on either blood pressure readings or arterial oxygen saturation were presented. The two patients with blood pressure drops in our spinal series suggest that hypotension reaching shock levels is followed by diminished liver function. Anoxia of the hepatic parenchyma seems the most likely explanation. This point is deserving of further study.

While our data on ether would appear to indict this anesthetic as a potential hepatotoxin, practical reasoning eliminates such a conclusion so far as patients with normal livers are concerned. The diminished liver function observed in our patients was only

a temporary one indicative of *functional* and not organic damage. While postoperative morbidity was more prevalent after ether, recovery was prompt and after two or three days the postoperative courses were the same for both the spinal and ether cases. On the other hand, given a poor risk patient whose liver function is subnormal due to probable organic damage the selection of an anesthetic would become a point of importance. It seems that spinal anesthesia, administered with measures to sustain blood pressure, would offer less hazard to the poor risk patient than ether administered by the open drop method. Our mortality statistics on patients with gallbladder disease undergoing cholecystectomy during the past fifteen years bears this out, although a decreased incidence of pulmonary complications following spinal anesthesia and better preoperative preparation for surgery undoubtedly are important factors in a decreased mortality.

Avertin analgesia as a basal anesthetic in patients with goiter produces a slight impairment of liver function. In mildly toxic goiters such a side effect is negligible, nevertheless, it is an effect on the liver that is not encountered following the administration of amyral and morphine for preoperative sedation. (Fig. 1.) Our limited experience with avertin suggests it may possess more pronounced hepatotoxic effects in toxic goiter.

A more practical disadvantage in using avertin as a basal analgesia in combination with novocain infiltration is absolute loss of co-operation during the operative procedure on the part of the patient. The majority of patients operated upon under avertin-novocain, though unconscious, required restraint to prevent involuntary thrashing movements. This is never encountered with the patient under amyral-morphine-novocain sedation during thyroidectomy. Much has been written about the "psychic trauma" incident to thyroidectomy under local. We had never quite understood this term until thyroidectomy was attempted under avertin-novocain. Psychic trauma was encountered then

face to face, not by the patient, but by the surgeon striving to accomplish a delicate task on an operative field that changed its locale every few minutes because of involuntary movements by an unconscious patient who, limp and snoring one moment, would all but climb from the operating table the next.

To be able to perform thyroidectomy on a conscious, quiet, co-operative patient is extremely advantageous to the surgeon. It is the only way he can judge accurately throughout the operation the patient's reaction to thyroidectomy. Any undue restlessness or tachycardia during the operation is a warning which permits alteration of the operative procedure accordingly. Many of our patients, prepared for bilateral operation, have been subjected to hemithyroidectomy only because their reaction on the table made it clear that they were not the bona fide risks we had considered them. Such evaluation of a patient with a goiter during surgery is impossible in patients rendered unconscious by an anesthetic. There can be little doubt but that this one important advantage of local anesthesia has been a great factor in a mortality rate of well under 1 per cent reported by us recently.<sup>7</sup>

#### SUMMARY

The effect of certain anesthetics and various operative procedures on liver function was studied in eighty-four patients before and after operation, using the hippuric acid test as an index of hepatic function. All of the patients studied were considered good operative risks and were without evidence of functional liver insufficiency before operation.

Spinal anesthesia produced the least evidence of hepatic dysfunction in twenty-one patients subjected to a variety of operative procedures. In eighteen patients (85 per cent) liver function averaged 104 per cent before operation and 96 per cent on the first or second day after operation. In two patients in whom a transient fall in blood pressure occurred on the operating table, the postoperative hippuric acid tests

fell to 74 and 49 per cent, respectively, and then returned to normal within seventeen days.

Ether anesthesia produced transient subnormal hepatic function in all of sixteen patients. An average liver function of 101 per cent before operation was reduced to 67 per cent. By the end of one week normal values were again obtained.

Avertin given as a basal anesthetic in combination with novocain infiltration reduced liver function by 5 to 30 per cent in seven patients.

Amytal and morphine given as preoperative sedation to forty patients operated upon under novocain infiltrated locally produced no change in the functional state liver as reflected by the hippuric of the acid test.

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# THROMBOCYTOPENIC PURPURA

JOHN ROBERTS PHILLIPS, M.D.

Visiting Surgeon,  
St. Joseph's and Memorial Hospitals

AND

MARTIN A. ZIONTS, M.D.

Visiting Physician,  
St. Joseph's and Memorial Hospitals

HOUSTON, TEXAS

THROMBOCYTOPENIC purpura is characterized by a diminution of the blood platelets. The first case was reported in 1735 by Werlhof. Brohm, in 1881, and Denys, in 1887, were the first to describe and emphasize that the essential finding was the lowered platelets in the peripheral blood. Hayem noted the normal clotting time and the absence of clot retraction. Duke, in 1910, showed the prolonged bleeding time. The first splenectomy for the condition was performed by Kaznelson in 1916.

Purpura hemorrhagica can be classified in many ways, but since we are only discussing thrombocytopenic purpura, we are limited to the symptomatic and the idiopathic type. Symptomatic purpura is that in which we find the purpura as an incidental finding or secondary finding along with the primary disease. This study was made on twenty-three cases, seven of these cases were of the symptomatic type and sixteen were of the idiopathic type. Eleven patients of the idiopathic type were splenectomized.

The various causes of the symptomatic type are: (1) blood dyscrasias, as leukemia, pernicious anemia, splastic anemia. In the series of cases studied there were three good examples of the type:

One was a four-year old white male admitted to the Hospital in 1941 with the symptoms of hemorrhages from the mouth and purpura. The blood findings were: platelets 11,500, white blood count 3,100 with 77 per cent lymphocytes, absent clot retraction, bleeding time five minutes. Splenectomy was performed; there was momentary rise in the platelet count, but the child did not improve. One month later the bleeding time was forty-nine minutes, the platelets 9,300, lymphocytes 88 per cent. One week later the white blood

count rose to 39,000 with 95 per cent lymphocytes and the diagnosis of leukemia was made. This was confirmed at autopsy.

Another case, a seventeen-year old male was sent into the hospital as a case of purpura, but the diagnosis of leukemia was proved before splenectomy was contemplated. Still another was a twenty-year old white female admitted to the Hospital in 1938 with purpura and bleeding from the gums of three to four months' duration. Examination showed bleeding gums, purpuric spots, and a nonpalpable spleen. The tourniquet test for capillary fragility was positive, platelets varied from 10,000 to 30,000, white blood count ranged from 2,000 to 3,800, clot retraction was absent, bleeding time was four minutes. On sternal aspiration no cells were obtained. Splenectomy was performed. The spleen was of normal size with a smooth capsule and prominent corpuscles. After the operation the patient oozed and oozed, was given transfusions several times but the hemorrhagic symptoms continued.

All three cases bring out a very important point, namely, unless all the findings of purpura are present and no other abnormal blood findings are present, hesitate to operate. In the two cases in which the diagnosis was finally made of leukemia, there was a leukopenia with a relative increase in the number of lymphocytes. In the third case, leukopenia and a sternal aspiration revealing no cells indicated the diagnosis of a possible aplastic anemia, hence the splenectomy should have been delayed for further studies.

2. Acute infections are sometimes accompanied by purpura with a thrombocytopenia as seen in typhoid, pneumonia, meningitis and occasionally with exanthemas. In this series there were two cases. One case was seen during the course of a rather septic pneumonia and the other in a small child with a large boil or carbuncle

of the neck. Both cases cleared rapidly with the healing of the causes of the thrombocytopenia.

3. Chronic infections also, are seen as a cause of a drop in the platelet count with resultant purpura. Tuberculosis and subacute bacterial endocarditis are the two chief offenders in this instance. There were no examples of this type in this series of cases.

4. Drugs are perhaps the most common cause of lowered platelet counts and the list of drugs which have been incriminated is a long one, but the most common are neoarsphenamine, quinine, sedormid, phenobarbital and the sulfonamides. An example of this is seen in a thirty-three-year old white female who was admitted in 1933 with a history of having intravenous injections for her syphilis for the three months previously. She had been menstruating for one month and on examination was pale, and had tenderness in the left lower quadrant. The white blood count ranged from 2,900 to 3,400; there was a marked anemia, the bleeding time was eight to fourteen minutes, the platelets were 4,000. She was given transfusions several times and the platelets slowly rose to 38,000. No follow-up was possible.

5. In cases of advanced malignancy with metastases to the bone marrow low platelet counts are sometimes seen.

6. In cases of splenomegalies such as Banti's, Gauchers or hemolytic icterus low platelet counts are detected. No cases of these last two types were seen in this series.

The idiopathic type of thrombocytopenic purpura is divided into two categories by the type of course they follow, namely, acute and chronic. The more common type of acute case is that which recovers for a while then goes on to a chronic form. Other forms are those in which there is a complete recovery and the patient is well completely. Some of these cases which appear as perfectly normal relapse after a varying length of time. Certain of the acute cases, in spite of all therapy, finally succumb, and in these cases various types of lesions may be found.

One type of that which Rosenthal calls megakaryophthisis in which there is a marked diminution of the megakaryocytes. In other cases one sees marked vascular changes with generalized small intravascular thrombi. In these fulminating cases the course of the disease may be very short as in the two cases reported by Denninger, wherein the entire elapsed time of symptoms was eight and one-half and eleven hours, respectively. In this series there were five acute cases with one fatality. This fatal case was one of the fulminating type, the child having symptoms for only thirty-six hours before the fatal termination. The other four cases recovered completely and left the hospital after transfusions.

The chronic type of idiopathic purpura hemorrhagica was seen in eleven instances and it is chiefly about these types of cases that this paper is concerned. This disease is most common in children and in young adults, especially girls. Of the sixteen cases, ten were in females whose average age was twenty-seven years. The etiology of the lowered platelets in these cases has been studied by many investigators and apparently there is more than one cause. Some of the workers believe that the vascular endothelium is injured and secondarily causes a fall in the platelets by causing their agglutination on the injured points. However, the majority of investigators are of the opinion that the essential factor is the platelets themselves and that they may be low in the peripheral blood because of poor production or by increased destruction. The lytic effect of the spleen on platelets was first suggested by Kaznelson in 1916. It is rather difficult to show phagocytosis of platelets in the spleen although it has been demonstrated. Poor production may be due to some substance elaborated by the spleen inhibiting the budding off of the platelets from the megakaryocytes, a sort of maturation defect; or it may be due to an actual depression of the megakaryocytes. This substance, thrombocytopen, has been demonstrated by Troland and Lee and recently

confirmed by Rose and Boyer. The majority of workers have been unable to confirm this.

The critical level of the platelets varies considerably in the opinion of various authors on the subject. However, in the great majority of cases purpuric phenomena occur when the platelet count is below 100,000. We believe that the best method for all practical purposes for the enumeration of blood platelets is the method of counting them in the blood counting chamber using a simple 3 per cent solution of sodium citrate as the diluent.

The symptoms of this disease are well known, they are: (1) hemorrhages into the skin, mucous membranes and internal organs. In these sixteen cases the most common site of the lesion was purpura of the skin and secondly, bleeding gums; (2) fever is not seen as a rule; though, in the acute cases this may be seen; (3) the spleen is only slightly enlarged although there are cases in which the enlargement has been pronounced; (4) when blood loss has been great, all the common symptoms of anemia will be present; (5) no adenopathy or hepatomegaly; (6) the white blood cell count is normal or there may be a slight leucocytosis with a normal differential or one which shows a slight increase in the polymorphonuclear count; (7) the platelets are diminished; (8) there is increased bleeding time; (9) absent clot retraction; (10) decreased capillary resistance, and (11) normal prothrombin time and coagulation time. This latter finding has been challenged by Nygaard who finds by his photo-electric technic that there is a delayed coagulation time in this disease.

In the chronic type, the platelets may be normal or decreased, though the capillary resistance and the tendency to bruise remain. One often sees exacerbations coinciding with the menses. Uterine hemorrhage may be the only symptom in these cases and the doing of the snake venom test is of differential value.

One should be on guard in those cases in which the amount of hemoglobin and red

blood cells is too low compared to the actual blood loss and in which leukopenia is present. In these cases a very careful differential count should be done to rule out aleukemic leukemia. Furthermore, a study of the bone marrow is of great importance for several reasons: (1) to determine if there be any form of leukemia present; (2) if there be an aplasia of the bone marrow, and (3) if there be a normal decrease in the number of megakaryocytes. Reticulocyte counts are of value to determine if normal red cell regeneration is taking place. In this series three cases of purpura with a leukopenia were found (exclusive of the two cases of aleukemic leukemia) and in these cases the results were not good. One patient was operated upon with death as a result. The other two patients continued to have purpuric phenomena.

Since many of these cases have bleeding from the gums as a chief symptom, they go to the dentist first; therefore, it is of vital importance that the dentist be cognizant of the disease. Outside of the sternal marrow study, all tests can be performed with ease and facility.

Wintrobe and his co-workers show that males as a rule recover from the first attack and hence the operation is more to be considered in females.

The differential of this disease is not hard if one recalls the necessary criteria that should be present. In the Henoch-Schoenlein type, joint pains and toxemia are frequent manifestations and these are not seen in the idiopathic type. Leukemia and aplastic anemia have been discussed. In hemophilia, there is a normal platelet count, normal capillary resistance, normal bleeding time and a marked prolongation of clotting time.

The spleen removed shows an endothelial proliferation of the Malpighian bodies and sinuses with an increase in the number of the reticulum cells throughout the whole organ. There is also seen an infiltration of polymorphonuclear eosinophiles and megakaryocytes. Occasionally, one sees phagocytosed platelets. In the bone marrow the

picture can be one of aplasia with megakaryopthysis normal with an anemia response of the red cell series or increased megakaryocytes with many young forms and poorly budding off of the platelets.

#### TREATMENT

Many types of medical management have been tried but most of them seem to have been of value only in the hands of the original investigators. Transfusion has been of value especially pre- and postoperatively and in the acute cases for whom operation is so dangerous. Many patients, especially children, have spontaneous remissions and remain well for the rest of their lives. This probably accounts for some of the results with some of the various medical methods of management in the acute cases. In some of the acute cases, the symptoms do not abate and one is forced into operating in order to attempt to save a life.

Treatment with calcium, vitamin C, vitamin K, horse serum, thromboplastin, foreign protein therapy, adrenalin injections, parathormone, x-ray and radium have all been tried with rather poor results in the hands of most of the men who have tried them. Snake venom has been used but there, too, the results have been none too good. But for a prognostic test the use of snake venom has been of some value. Cases in which the intracutaneous test became negative after treatment with snake venom responded well to splenectomy.

The most effective treatment is splenectomy. Ligature of the splenic artery was tried in two cases by Rosenthal and Berg and found to be of no value. As to pre-operative care (1) be absolutely sure by all the tests at your command that this is a case of chronic idiopathic thrombocytopenic purpura, and (2) preoperative blood transfusion and preparation for postoperative transfusions should be provided. The operative technic will not be discussed except to mention one important point, namely, that no accessory spleen be left *in situ* to continue on with the mischief. Some of the poor results are undoubtedly due to

overlooking this point. Hesitate before thinking too seriously of going back in to stop a bleeder that you imagine may be present in some of the more stormy cases.

The results in the acute cases in which operation was tried carried a much higher mortality (70 to 80 per cent). In chronic cases in which operation was performed the results were excellent with only 8 per cent mortality. In this series none of the patients with acute cases was operated upon. In the eleven chronic cases in which splenectomy was performed there were nine complete cures, one with symptoms remaining as before the operation but still alive after eight months. There was one death. The patient who died did not have as complete a workup as we would like to have seen in order to assess the case better. Two of the patients in this series had accessory spleens. The results of splenectomy as summarized by Rosenthal can be placed under the following groups: (1) complete recovery, (2) symptomatic recovery but platelets diminished in number, (3) complete recovery with a very high platelet count (thrombocythemia), (4) partial recovery with mild hemorrhages and thrombocytopenia, (5) persistent anemia with normal platelets and no hemorrhagic state, (6) unsuccessful splenectomy with partial recovery and then death, and (7) unsuccessful outcome with early post-operative death.

The following is the case history of a patient recently observed by us:

The patient, a nineteen-year old white female, three years ago first noted black and blue marks over her entire body. Thyroidectomy for hyperthyroidism was performed two and one-half years ago with no undue bleeding. One and one-half years ago she noticed a sudden increase in the bruising tendency. There never was any excessive menstrual flow. She was seen by several physicians and the following types of medical treatment were tried: blood intramuscularly, vitamin C, vitamin K, calcium and snake venom. After each new type of treatment there was an apparent improvement but the condition remained with her and

gradually became worse. Studies done at that time showed the following: platelet count never below 177,000, bleeding time seven to ten minutes, absent clot retraction, positive tourniquet test. Sternal marrow aspiration reported as normal.

When one of us (M. A. Z.) first studied her case she had the following: multiple ecchymoses, petechiae and some small hematomas. The spleen was not palpable. There was only a mild anemia. There was a normal white blood count and differential count and a normal bone marrow study. The bleeding time was six and one-half minutes. There was no clot retraction, a positive tourniquet test was present. The platelet count (chamber count) was 30,000. Splenectomy was performed several days later by one of us (J. R. P.). The spleen was just a trifle enlarged, the corpuscles were quite prominent. The platelet count post-

operatively rapidly rose so that on discharge they were within normal limits; no new petechiae or ecchymoses developed. Today she is symptom free and her platelet count is normal.

#### SUMMARY

We have presented twenty-three cases of thrombocytopenic purpura, sixteen of which are idiopathic—the case for splenectomy. Eleven of these were chronic cases and were splenectomized. Seven were symptomatic and we believe that splenectomy in this group is not indicated.

The diagnosis is usually certain when care and attention is paid to the diagnostic criteria as set forth. Likewise when the diagnosis is certain splenectomy gives good results with small risk.



# THE MODERN TREATMENT OF OSTEOMYELITIS\*

HENRY W. MEYERDING, M.D. AND

Section on Orthopedic Surgery,  
Mayo Clinic

REED S. CLEGG, M.D.

Fellow in Orthopedic Surgery,  
Mayo Foundation

ROCHESTER, MINNESOTA

THE use of chemotherapy in cases of osteomyelitis has led to revolutionary changes in the management of treatment for the disease. Pyogenic organisms that cause osteomyelitis pass through the blood stream to become localized, thus producing abscesses and destruction of bone with disabling results. The prevention and sometimes the cure of early osteomyelitis may result if chemotherapy is administered thoroughly during the stages when the infection of the blood stream or septicemia is recognized and if the treatment is instituted before abscess formation has taken place.

Osteomyelitis may be extensive, involving the medulla, cortex, periosteum, metaphysis and epiphysis or it may be limited to any one of these parts. The most frequent predisposing causes are low resistance accompanying disease, trauma, foci of infection and inflammatory lesions about the skin or nails where bacteria can enter the blood stream and extend into bone. Bacteria occasionally reach bone by direct extension. Septicemia may first be present and bacteria localizing in the end arteries of bone may produce osteomyelitis.

It is accepted generally that staphylococci, especially *Staphylococcus aureus* and *Staphylococcus albus*, are the exciting micro-organisms in 80 to 90 per cent of all cases of osteomyelitis and that streptococci are responsible for most of the remainder. Except for the more extensive course of infection caused by *Staphylococcus aureus*, there is comparatively little variation in the pathologic changes in infections caused by pyogenic organisms. The virulence of the organism varies and, in some instances,

as illustrated by Brodie's abscess, staphylococci exist and produce osteomyelitis in a semidormant state.

Among adult patients osteomyelitis originates in any portion of bone but when the disease affects children it usually begins in the diaphysis of the long bones, especially in the femur and the tibia. Bacteria lodge in the fine capillaries or end arteries of the long bones, where toxins produce vascular engorgement, edema, leukocytic infiltration and necrosis. The infection rarely penetrates cartilage but spreads through the haversian and Volkmann's canals to the cortex and subperiosteum. It frequently cuts off the vascular supply of portions of bone and causes absorption which is associated with sequestration and subperiosteal abscesses.

Among the first symptoms of acute osteomyelitis are diffuse aching pain in the involved region, which subsequently becomes localized, tenderness, increased heat and protective muscle spasm. Such general symptoms as fever, malaise, headache, nausea and vomiting are usually present. In many cases of chronic osteomyelitis there is a persistent draining lesion which does not produce untoward effects except occasional exacerbations of pain by temporary obstruction of drainage. Although osteomyelitis may remain inactive and for a number of years may appear to have healed, there is always a potential danger of recurrence.

The early recognition of osteomyelitis is often dependent upon evaluation of the clinical history of a few vague symptoms, since localized signs or roentgenographic changes are not present during the early

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stages. Roentgenographic changes may not occur during the initial eight to ten days, but from the tenth to the fourteenth days a region of decreased density or ill defined patch will usually be visible near the epiphyseal line; definite softening and periosteal reaction occur after two to three weeks. Subsequent roentgenograms at monthly intervals may reveal thickening of the shaft, rarefaction, sequestration and involucrum as the condition progresses. The diagnosis of osteomyelitis usually is not difficult, but in some instances an exploratory operation and the removal of a specimen for microscopic and bacteriologic examination may be necessary to distinguish osteomyelitis from osteitis, periostitis, arthritis and various other inflammatory conditions or tumor. The marked similarity of hemangio-endothelioma and osteomyelitis cannot be overemphasized. This similarity has been considered by Pollock and one of us (H. W. M.) in a previous paper. The local findings, especially the roentgenographic findings, and the general symptoms, even moderate fever, may be so similar in cases of osteomyelitis and of Ewing's tumor that diagnostic irradiation or biopsy is necessary in order to distinguish between the two conditions.

One must take into consideration several factors when determining the type of treatment indicated in an individual case, namely, the duration of disease, the site and extent of the lesion, the causative organism and the general condition of the patient. There are few contraindications to the usual supportive measures such as complete rest in bed, immobilization of the affected part, the use of analgesics, sulfonamides and the abundant ingestion of fluids. There is some difference of opinion, however, regarding the advisability of surgical intervention in cases of acute osteomyelitis. Although most authors still advocate immediate incision and drainage and the instillation of petrolatum packs (Orr's method of treatment) or the use of dakinization, some believe that incision of

periosteum and soft tissue abscess is preferable. The lessons gained from the first World War taught the effectiveness of



FIG. 1. Ewing's tumor of upper portion of shaft of right femur.

dakinization of infected wounds. In order to obtain successful results with this method of treatment it is essential that the patient receive meticulous care; all dressings must be changed under rigid aseptic conditions and the edges of the skin protected with petrolatum gauze.

Recent studies have revealed the increasing value of chemotherapy as an adjunct in both the conservative and the operative treatment of osteomyelitis. In the early stages of some of the indefinite inflammatory lesions and in cases of septicemia in which the infection is not localized, the immediate use of chemotherapy doubtless lessens the severity of the local and general manifestations and is a life-saving measure. Sulfanilamide and sulfathiazole, which are known as sulfonamides, should be used in the prophylaxis of severe wounds and

compound fractures, in cases of osteomyelitis in which operation is contraindicated or refused, in preoperative and postoperative



FIG. 2. *a*, chronic osteomyelitis of approximately forty years' duration. There is marked thickening of the femur with regions of sclerosis and osteoporosis and evidence of repeated operations; *b*, lateral view.

treatment and in cases in which a fulminating infection is associated with septicemia.

Sulfanilamide apparently is more effective than sulfathiazole in the treatment of infections caused by streptococci, while sulfathiazole is the drug of choice in the treatment of staphylococcal infections. These drugs are especially effective in cases in which septicemia is a complicating factor. They may be safely and effectively administered orally in the form of tablets, each containing  $7\frac{1}{2}$  gr. (0.5 Gm.). Ninety gr. (6 Gm.) should be administered in six doses. This amount usually will maintain a concentration of 10 mg. of the drug in each 100 cc. of blood. When higher concentrations of the drug are maintained in cases in which virulent infection does not respond well to treatment, the patients should be observed carefully for untoward symptoms. Some physicians advocate the administration of huge doses of these drugs during the first twenty-four hours, that is, until the

concentration of the drug in the blood reaches 20 to 30 mg. per 100 cc., and the maintenance of this concentration for two to three days, after which the amount is decreased progressively in proportion to the progress of the patient. It is too early to evaluate definitely the efficiency of this plan of therapy. The local administration of 10 to 15 Gm. of the powdered drug is indicated as an adjunct in the treatment of open wounds. There does not appear to be any irritation of the surrounding tissues following local application of these drugs, and the amounts employed do not play a great part in the concentration of the drugs in the blood. These drugs can be injected into the sinuses or cavities when mixed with cod-liver oil; 5 Gm. of either drug is blended with 30 cc. of the oil. Either sulfanilamide or sulfathiazole can be used in a standard 0.8 per cent solution for the irrigation of wounds. There are some physicians who claim that this solution has a bacteriostatic or bacteriocidal effect. The use of this type of treatment varies according to the type of infection and the individual response to the drug used. In cases of septicemia in which treatment is adequate, the recovery rate is 70 to 75 per cent.

Sufficient time has not elapsed to permit evaluation of the types and extent of acute and chronic poisoning resulting from chemotherapy; we have encountered instances of individual hypersensitivity to chemotherapy but not any case in which serious permanent damage occurred. Such untoward reactions as malaise, headache, nausea and vomiting, and gastrointestinal derangements are usually tolerable and may be partially prevented by inhalations of oxygen.

#### REPORT OF CASES

The following reports of cases illustrate the use of some of the methods of treatment that have just been described and also emphasize the difficulties encountered in the diagnosis and clinical management of some infections of bone.

## EWING'S TUMOR OF THE RIGHT FEMUR

CASE I. A boy, aged nine years, was brought to the clinic on August 8, 1938, because of



FIG. 3. *a*, region of periostitis with region of decreased and increased density in shaft of right femur; *b*, lateral view; *c*, anteroposterior view showing abscessed cavity with tube inserted and operative window; *d*, lateral view similar to *c* showing window through cast.

recurring attacks of nausea, vomiting, temperature ranging up to 102.2° F. and pain in the right thigh. The history did not disclose trauma or any other significant findings. The illness had begun fourteen months prior to the patient's admission. During this period attacks had occurred at intervals of several weeks and had lasted one to four days. A diagnosis of osteomyelitis of the right femur had been made clinically. Five months before the patient was brought to the clinic an exploratory operation had been performed, at which time the local pathologist had sent sections to a distinguished pathologist, who made a diagnosis of sclerosing osteomyelitis. Drainage had not occurred after the operation but pain and fever had persisted and three courses of roentgen therapy had been given.

Examination at the clinic disclosed a thin and undernourished patient who walked with a noticeable limp on the right and who had muscle spasm and swelling of the right thigh with limitation of motion of the right hip and knee. His temperature ranged between 99° and 100° F. The roentgenograms of the thorax

gave negative results. There was considerable variation of opinion regarding the diagnostic significance of the roentgenograms of the right

femur. The roentgenologist said, "This case brings up the perennial question of inflammation versus neoplasm." One of us (H. W. M.) expressed the opinion that the roentgenologic appearance was strongly suggestive of Ewing's tumor and advised against further operation but suggested irradiation as a diagnostic and therapeutic measure. Four courses of irradiation consisting of four treatments each were employed over a period of three months.

When the patient was re-examined at the clinic on December 6, 1938, râles had developed in the thorax and roentgenologic examination disclosed metastatic involvement of the lungs. This was four months after his first consultation at the clinic and nine months after surgical exploration elsewhere. The patient continued to fail and died at home on February 12, 1939, about twenty-one months from the onset of his symptoms.

Necropsy disclosed an extensive primary Ewing's tumor (hemangio-endothelioma) of the right femur (fig. 1) and metastatic involvement of the lungs, pleura, pelvis, ribs and skull.

*Comment.* This case illustrates the difficulty encountered in distinguishing inflammatory lesions of bone from neoplasms.



FIG. 4. Six and a half months after onset of extensive osteomyelitis of left radius with sequestration.

The cortical thickening, the extensiveness of the involvement and the periosteal lamination were suggestive of Ewing's tumor but osteomyelitis could not be excluded. Tissue removed in cases of Ewing's tumor has been diagnosed frequently as inflammatory. Irradiation causes marked regression of the local growth, an effect so typical as to lead to employment of the treatment as a diagnostic procedure; hence the term, "diagnostic irradiation."

#### OSTEOMYELITIS OF FORTY YEARS' DURATION

CASE II. A man, fifty-one years of age, formerly a patient at the clinic, returned for examination on June 27, 1941, because of pain in his right leg associated with a pulsating sinus which was discharging foul-smelling fluid. Since the onset of his trouble in 1916, approximately twenty-six years previously, this patient had had, at the clinic and elsewhere, numerous operations, among them curettage and sequestrectomy, and various forms of treatment, including treatment with maggots. Cultures had been made at various times and had showed staphylococci and streptococci. One of us (H. W. M.) had advised the patient on several occasions to have amputation because of the chronicity, stiffness of the knee, pain, foul-smelling discharge and the possibility of malignant disease, but he had refused.

Examination of the patient in June, 1941, disclosed that he was extremely ill, toxemic and feverish. Chemotherapy was instituted and on June 27, we performed amputation through the junction of the middle and lower thirds of the right femur. The soft tissues of the leg were a firm mass of sear tissue and the femur was several times its normal thickness as a result of chronic osteomyelitis. (Fig. 2A and B.) The patient's health improved after the amputation and at the time this report was written he had gained in weight, had complete relief from pain and the stump was healed.

*Comment.* One of us (H. W. M.) followed this case over a period of many years and from time to time was consulted by the patient because of the foul discharge, pain, fever and disability. He found it possible to control the odor by irrigations of Dakin's solution. The sinal cavity was so large and the disease so extensive that conservative surgical intervention was of little value and the repeated operations which the patient underwent served only to provide more adequate drainage. Amputation was the final choice and was resorted to only after prolonged illness, loss of function of the knee joint, disability and toxemia.

In this case, because of the prolonged irritation at the point of drainage the possibility of malignant disease was considered

but careful examination by a pathologist at the clinic failed to show any evidence of it. Since chronic osteomyelitis with prolonged drainage is rare, our experience with such cases is limited, but we have noted that malignant disease develops in cases of infection of bone associated with prolonged drainage; it occurs along the edge of the sinus and usually, when a specimen is removed for microscopic examination, is found to be epithelioma.

**CASE III.** A man, aged twenty-nine years, reported for examination at the clinic on October 1, 1940, at which time he complained of pain about the right knee of one month's duration. At the age of ten years he had had osteomyelitis of the left tibia which had completely healed. Thereafter he had been in normal health until, five weeks prior to registration, he had injured his right knee. Pain about the knee had begun one week after the injury was received, had been continuous, worse during the night, and had progressed in severity despite treatment. The physician in the home locality had considered a diagnosis of neuritis and two teeth which he believed were possibly foci of infection had been extracted. Because the patient's temperature had risen to  $103^{\circ}\text{F}$ . he had been hospitalized and had received 90 gr. (6 Gm.) of sulfanilamide daily for five days. At the end of this time roentgenographic examination, which previously had given negative results, revealed a region of decreased density in the femoral shaft, and the patient came to the clinic for consideration of surgical intervention.

Examination revealed evidence of local heat, swelling, tenderness and limitation of motion of the right knee. The temperature and the leukocyte count were normal. The sedimentation rate was 107 mm. per hour. The pain became more severe, the leukocyte count increased to 15,700 per c.mm. of blood, the temperature ranged from  $100.5^{\circ}$  to  $102^{\circ}\text{F}$ . and at the same time the roentgenograms definitely revealed osteomyelitis of the lower portion of the right femur. (Fig. 3A, B, C and D.) It was evident that chemotherapy had not checked the osteomyelitic process. The pain, temperature and increasing leukocyte count were signs that the infection was still active and that drainage was indicated.

At operation considerable thick purulent material was obtained and sent for culture.

Sulfanilamide powder and drains were inserted into the wound. Figure 3C and D reveals the postoperative appearance of the femur with



FIG. 5. Anteroposterior view three months after onset of acute osteomyelitis of right tibia which was treated by drainage and chemotherapy.

drainage tubes in place. The patient was dismissed eight weeks after operation, at which time the wound was practically healed.

The bacteriologic examination of the material removed at the time of the operation did not reveal any growth of organisms. The sterile cultures were of particular interest in that the patient had received a course of sulfanilamide prior to operation.

On August 12, 1941, ten months later, when one of us (H. W. M.) saw the patient he had

full motion of the knee, the wound was healed and he was not experiencing difficulty.

CASE IV. A girl, aged eleven years, was

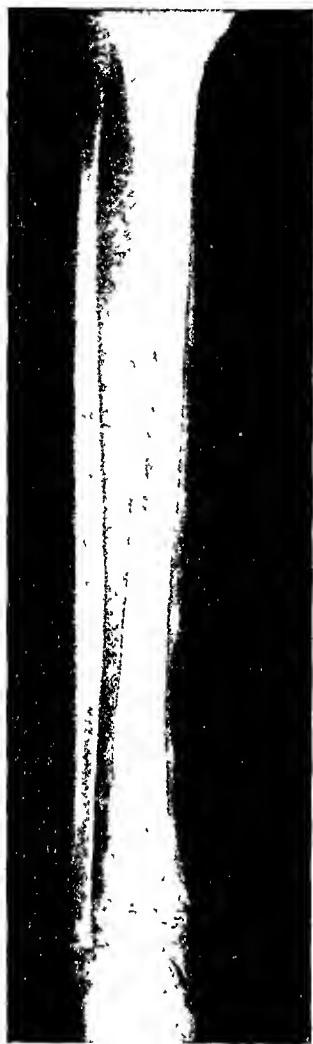


FIG. 6. Two months after onset of osteomyelitis of right tibia. Note involvement of entire diaphysis with regions of increased density and periosteal proliferation but no definite sequestra.

examined at the clinic on September 7, 1939, because of severe pain of four days' duration in the left wrist. One week prior to her admission a furuncle of the right buttock had been noticed; this lesion drained spontaneously five days later. Three days prior to her admission the patient had sprained the left wrist; on the following day pain had developed in the wrist and within forty-eight hours the girl's temperature had risen to  $105^{\circ}\text{F}$ . She vomited fre-

quently, became irrational and semicomatoso and was sent by ambulance directly to the clinic from a neighboring state for emergency treatment.

Examination revealed an acutely ill and delirious young girl who had swelling and tenderness of the left wrist and diffuse infection of the left forearm. At the time of her admission her temperature was  $104^{\circ}\text{F}$ ., the pulse rate 94 beats per minute and the leukocyte count 16,900 per c.mm. of blood. The leukocyte count increased to a level of 40,600 per c.mm. on the fifth day, at which time cultures of material from the furuncle of the buttock and of the blood were positive for *Staphylococcus aureus*. The patient received 60 gr. (4 Gm.) of sulfapyridine daily, an amount that maintained a concentration of 3.3 mg. of the drug in each 100 cc. of blood. Two days later through-and-through drainage of the forearm was instituted surgically, and cultures again revealed *Staphylococcus aureus*. Fluid was not obtained from lumbar puncture repeated several times. Roentgenograms taken during the first three weeks were negative but those taken October 16, showed extensive osteomyelitis of the shaft of the radius and destructive arthritis of the radiocarpal joint. Convalescence in the hospital was stormy and during this time several sequestra sloughed from the forearm. The patient's mother wrote us on February 14, 1941, however, that the arm had continued to heal and drained only occasionally. (Fig. 4.)

*Comment.* This case is a classical illustration of acute osteomyelitis and staphylococcal septicemia complicating a staphylococcal infection of the buttock. Chemotherapy in this case perhaps would have been more effective had a higher concentration of the drug in the blood been maintained during the acute stage of the disease. Had sulfathiazole been in use at that time, it would have been administered. Although the question of the advisability of surgical drainage in acute osteomyelitis in the presence of fulminating staphylococcal septicemia is debatable, we believe that under such circumstances drainage of a formed abscess is indicated, as the abscess is a possible focus of infection for an indefinite length of time. Treatment with sulfonamides, in our opinion, has proved

revolutionary in the management of such cases.

**CASE V.** A woman, aged forty-two years, was admitted on December 29, 1937, at which time she stated that she had been in normal health until one week prior to admission, when a wisdom tooth had been extracted. She further stated that twelve hours later pain had developed in her right knee and had become progressively more severe, that her temperature had ranged up to  $104^{\circ}\text{F}$ ., and that on the third day she had also intense aching pain in the left arm, sternum and back. A slightly productive cough had been noted.

Examination of this patient revealed tenderness and swelling of the right knee, a temperature of  $102.6^{\circ}\text{F}$ ., a leukocyte count of 13,000 per c.mm. of blood, many carious teeth and a wound of the jaw from the recent dental extraction. The patient was hospitalized and 60 gr. (4 Gm.) of sulfanilamide were given daily for eighteen days during which time a concentration of 3 mg. of the drug per 100 cc. of blood was maintained. The roentgenograms of the right lower extremity taken during the first two weeks were negative; those next taken revealed definite rarefaction in the shaft of the right femur. Several blood cultures made during the first two weeks of hospitalization were reported as negative, but subsequent to exploration of the lower third of the right femur on January 12, 1938, *Staphylococcus aureus* was found in cultures of the blood and of the material from the wound. The convalescence was stormy and despite all available medical aid, including six transfusions of blood and chemotherapy, there was a gradual downhill course until death occurred on the eighth day after operation, or the twenty-sixth day after extraction of the wisdom tooth.

**Comment.** It is possible that maintenance of a higher concentration of sulfanilamide in the blood might have been more effective; with our present knowledge of chemotherapy we would recommend sulfathiazole in large doses. Fortunately, such fatal complications as occurred in this case are becoming comparatively rare as knowledge of chemotherapy advances.

The following two reports of cases are added to illustrate advancement in the use of chemotherapy.

**CASE VI.** A boy, aged nine years, was examined at the clinic on May 7, 1941, at which time he complained of pain, swelling and redness of the right leg of five weeks' duration. The illness had begun spontaneously and had first been treated as rheumatism by the family physician. There had been progression of the symptoms accompanied by high fever. Although sulfanilamide had been administered for seven days, on the tenth day there was copious purulent drainage from the medial aspect of the lower third of the right leg. Roentgenograms at that time revealed osteomyelitis and the patient was brought to the clinic.

Examination of the patient revealed a thin, pale boy who had draining osteomyelitis of the right tibia. The temperature was  $100.5^{\circ}\text{F}$ ., the pulse rate 105 beats per minute, and the respirations were 25 per minute. The concentration of hemoglobin and the erythrocyte count were somewhat decreased and the leukocyte count was 11,400 per c.mm. of blood. The results of urinalysis, roentgenograms of the chest and a flocculation test were normal. Bacteriologic examination of material obtained from the draining wound revealed *Staphylococcus aurusc*.

The patient was hospitalized at once where he received 60 gr. (4 Gm.) of sulfathiazole orally each day for six days. The roentgenograms at that time revealed extensive involvement of the entire right tibia but clinically there was marked improvement in the boy's condition. On May 12, 1941, with the patient under general anesthesia the wound was enlarged and through-and-through drainage established. A few days later the boy was permitted to return home under the care of his family physician.

Examination at the clinic three months later revealed the presence of some serous drainage; the patient's general condition was much improved and roentgenograms disclosed extensive involvement of the entire shaft of the tibia without definite sequestration.

**Comment.** We believe that the course of the osteomyelitis of the tibia in this case was greatly influenced by the institution of chemotherapy, proof lying in the improvement shown, in the lack of extensive sequestration and in the type and amount of drainage. (Fig. 5.)

CASE VII. A girl, aged eleven years, was examined at the clinic on June 12, 1941, at which time she complained of pain about the right ankle joint. Eight days prior to her admission the patient had turned her ankle and the local physician had taken roentgenograms which proved to be negative. A cast had been applied to the right leg but had been removed five days later because the leg had become red and swollen and the patient's temperature had increased to 102.5°F. Forty gr. (2.6 Gm.) of sulfanilamide had been given to the patient and she had been referred to the clinic.

Examination revealed a temperature of 99.4°F., a pulse rate of 100 beats per minute, and marked heat, tenderness and swelling of the right leg. Roentgenograms were indeterminate; a clinical diagnosis of osteomyelitis was made and the patient hospitalized. Seventy-five gr. (5 Gm.) of sulfathiazole were administered daily for a period of eleven days. Clinically, there was definite improvement in the girl's condition but a temperature of 99° to 101°F. persisted. Roentgenograms at that time revealed typical osteomyelic destruction of the distal end of the diaphysis of the right tibia. The patient was dismissed to the care of her physician at home with the advice to take 60 gr. (4 Gm.) of sulfathiazole daily and to report back to the clinic in one week.

Subsequent examinations revealed continued improvement in this patient's condition and chemotherapy was discontinued August 8, 1941, after which efforts to build up her general resistance were begun. Roentgenograms eight weeks after the onset of the condition revealed involucrum but no sequestration. (Fig. 6.) The reaction disclosed by the roentgenograms was decidedly less in extent than that which we have observed in cases in which chemotherapy has not been used.

*Comment.* This case illustrates the improved results obtained from adequate chemotherapy in cases of acute osteomyelitis. It is our opinion that sulfathiazole was

effective in the prevention of extensive destruction of bone with sequestration, which is the usual complication in such cases.

#### SUMMARY AND CONCLUSIONS

Chemotherapy orally and locally is indicated in osteomyelitis complicating fractures. Chronic osteomyelitis of a low degree of virulence may be in existence over long periods of time, may go unrecognized, and usually is diagnosed as arthritis. In the majority of instances roentgenograms will reveal localized circular or oval areas of decreased density. Furthermore, the nonsuppurative sclerosing type of osteomyelitis (Garre's type) is characterized by a region of localized increased density of bone with thickening of the cortex and medulla, and is accompanied by persistent pain which is worse at night; the leukocyte count is not increased and localized heat may or may not be present.

We believe that sulfonamides have proved of inestimable value in the treatment of septicemia and acute osteomyelitis. Blood cultures taken before localization of the lesion of the bone and adequate chemotherapy may prevent osteomyelitis and its complications and septicemia with fatal results. When large abscesses have formed, it is our opinion still that adequate surgical drainage of the infected region is indicated.

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# END RESULTS OF SCREW FIXATION IN INTRACAPSULAR FRACTURES OF THE NECK OF THE FEMUR

T. TURNER THOMAS, M.D.

PHILADELPHIA, PENNSYLVANIA

**I**N our opinion the old classification of fractures of the femoral neck into the extracapsular and intracapsular remains the best. The intracapsular is for us decidedly the more important of the two. This is because of our failures to obtain bony union of the fragments except by screw fixation.

## EXTRACAPSULAR FRACTURES

While these fractures are probably if not in all cases partly intracapsular anteriorly, they are essentially extracapsular because the joint is invaded if at all very close to the anterior intertrochanteric line, which is the lowest limit of the capsule and synovial cavity. In other words, the fracture line passes through the base of the neck, which is largely made up of cancellous bone; so that the fragments present wide fractured surfaces, usually with good approximation and a capacity for much callus formation, so that good union occurs almost always. The opposite is true of the intracapsular fracture, the small head fragment of which has a much poorer blood supply coming only through the ligamentum teres. That of the extracapsular fracture gets as much blood from the ligamentum teres, and in addition has much more ligamentous and muscular attachments through which to receive additional blood supply. The callus and other resulting reparative material developed, probably fill up the small part of the joint involved and wall off the fracture from the joint, so that it presents a much less troublesome problem than the intracapsular fracture. I cannot recall nonunion in an extracapsular fracture. In my experience the Whitman abduction cast applied early has almost always produced a well nigh perfect reduction and

close approximation of the fragments, with resulting firm bony union and excellent function, so that we feel little concern about the prognosis in these cases.

## INTRACAPSULAR FRACTURES

Of all common fractures of the extremities these have been the most formidable from the standpoint of providing a good prognosis. In recent years they have received much attention and have made much progress in the results obtained. I have been interested in fractures for forty years with a very limited early personal experience and only a moderate one since. This discussion will be limited almost exclusively to personal experience since 1918, and will deal almost entirely with the methods used and the results obtained with screw fixation of the fragments. It is believed the best presentation can be made by cases selected because of their particular importance in emphasizing the essential facts.

My particular interest in intracapsular fractures has been largely influenced by a case in a sixty-year old man, who was admitted to the Northeastern Hospital May 10, 1920, four weeks after his accident. An amputation had been done at the middle of the opposite thigh years before. He was a maker of fine instruments but needed one good lower limb in order to follow his occupation with the support of a crutch. I did not have enough confidence in the Whitman abduction cast to rely on it for bony union in this case after a four weeks' delay elsewhere in beginning treatment.

Delbet had passed a screw through both fragments without arthrotomy, but I could not then find a satisfactory description of

his method of introducing the screw. He depended upon traction for the correction of the displacement of the fragments and a specially devised apparatus for accurate placing of the screw. If I had found a satisfying description of the method I could not have obtained the instrument in time for use in my case, so that I was compelled to abandon the method or quickly develop another. This method devised for screw fixation for this case has been employed in every other patient operated upon since, consequently, I cannot discuss any other operation for the condition. It was reported before\* with the results in four cases. All the patients were operated upon from four weeks to four months after the accident and all had excellent functional results, particularly in view of the delay in each one. The first and only failure to obtain union by the method will be discussed later.

That the methods without arthrotomy and exposure of the fragments have had a strong appeal, is evidenced by the variations in the methods attempted. It could not be otherwise with so radical a departure from the established procedure for applying internal fixation of a fracture, particularly one within a joint and more particularly a joint so difficult to expose. But if it can be done more safely than by the direct exposure, in all probability it will be done more frequently with increasing efforts to improve the method and with a consequent delay of standardization. There are too many problems to be settled, too many questions to be answered. We are content to follow our own method until convinced another is better. A better one must be safer and produce a better result. Ease of performance can afford to wait.

When the need of devising it arose unexpectedly, the most trusted method for obtaining bony union was the Whitman abduction cast. According to our experience, it was then and is now the only method of reducing the deformity without traction almost if not perfectly every time, which it will continue to maintain until the

cast is removed. We know of no other method which will do this except the Whitman, around which the screw fixation was devised. If for any reason we were deprived of this advantage, the method would be abandoned. There was only one way of retaining it. It became necessary to operate through an opening in the cast. To the objection that one could not provide enough room for performing the operation, the reply is that it has never been done by us in any other way; and to the objection that it exposes the patient to the danger of infection, the answer is that no evidence of infection can be recalled in any case, not even a stitch infection. That the x-ray taken after the drying of the cast would show the position of the fragments until the cast was removed, was vital to the safe placing of the screw. One other requirement was essential, namely, provide before the operation sterilized screws of the proper length and caliber. It will be too late to select and sterilize others during the operation. We think it would be impractical to provide a sufficient number of specially devised screws to meet any emergency in this operation. There will be too great a variety of requirements in length and caliber in the different sizes of patients. The method necessitates having ready at the moment of need, the necessary number of any desired screw. If these requirements could not be provided, it would be necessary to abandon the operation. We think it can be done only with the common carpenter screws, which are made of steel can be sterilized as thoroughly as the best special screws made. That is all that matters in connection with this operation or any other fracture we can recall, except those in which special plates and screws were employed. We have used few or none of these for years. Of the common screws one can obtain any number, length or caliber at almost any time in almost any town. Without these screws the operation becomes impractical, but we have been using them for more than twenty years and can recall no cause for regretting it. The operation

\* Am. J. Surg., p. 292, September, 1921.

requires it and we prefer the operation to any other with a special screw, at least in such operations as these. Without ever regretting it, we employed the common screws and nails in other fractures before doing so in those of the femoral neck.

Having decided the approximate length of screw desired from the x-ray film, with the necessary correction for the enlargement produced by the x-ray and the desired caliber, enough are selected of the correct length and caliber. At least the next lengths above and below are selected and several calibers of each. The one or two used must cross the fracture line sufficiently to grasp the small fragment firmly but not pass through the head into the joint or acetabulum. The screws must be selected and prepared so that they will work successfully when introduced; for if they fail as already stated, it will be too late to select and prepare new ones.

*Method of Screw Fixation.* A Whitman abduction cast is applied in the usual manner without inclusion of the opposite limb. An opening is made in it over the great trochanter with an old Bard-Parker knife blade while the cast is still soft, about nine inches long and about six inches wide, with the trochanter about in the center. The operation is done through this cast opening; because it is the only method available for utilizing the guarantee of the cast for perfect reduction and fixation of the fragments until the screws are introduced and union established. Just as we have banished the fear of too much traction in the use of the traction cast, so we have banished the fear of infection in these cases. It could happen but never has in the twenty years of our use of the method. Why let that fear deprive us of the advantages of the operation?

A few years before our first screw fixation in these cases, we adopted open reduction and internal fixation for most shaft fractures of the lower extremity, because of our failure to accomplish satisfactory reduction by the closed method. We then

became interested in the practice of an other surgeon in similar operations. He swabbed the wound before closure with dichloramine-T with the purpose of destroying or discouraging the growth of any bacteria that might have survived the preparation of the field of operation or gained admission to the wound during the operation. Without knowing how much if any bactericidal value it has we have not yet discontinued the practice, although we have substituted for the dichloramine-T a 2 per cent tincture of iodine followed by alcohol. We think these two, along with the perfect continuous immobilization of the fragments and a simple straight incision to the bone with almost no dissection of the tissues, will have much influence in preventing infection.

*Instruments and Screws.* The only instruments are those necessary for an ordinary six-inch incision over the great trochanter to the bone, which need be exposed only enough over the trochanter and the shaft of the femur a few inches lower to feel the surface for the introduction of the screws. We are not anxious to expose the bone widely to see all parts of the bone in this area. Several metal screw drivers, retractors, hemostats, catgut, etc., and other necessary material for such an operation must be available as usual. The screws must be of the desired length to grasp the head fragment firmly without going in too far. The length is determined by the distance on the x-ray film from the external surface of the bone, about a half inch below the well defined lower border of the great trochanter, which can be easily felt and seen in the wound and more easily in the x-ray film, to within about a half inch of the most prominent articular surface of the head. This distance could vary with the degree of rotation of the femur during the application of the cast. This length is then reduced a half or five-eighths of an inch to compensate for the x-ray enlargement of the head. If the limb is always held in forced internal rotation as usual in the application of the cast, this variation will

be slight and the plane of the path of the screw will be almost if not completely horizontal, which is most easily followed in imagination for the blind introduction of the screw.

Two screws of the selected length are usually introduced. The others prepared vary in their lengths and calibers above and below the length and caliber selected. These additional screws are considered the most favorable for substitution if the x-ray taken during the operation indicates a faulty length, i.e., too long or too short. We prepare several of the length selected and likewise several of each length above and below that. In the same manner several calibers of each length above that of the first introduced, will be necessary if the first must be removed, because the substitute screw must always be larger than the one removed in order that it may take a firm hold on the surrounding bone. This is the most complicated feature of the operation but we have not yet been able to simplify it. The screw must take a firm grip on the bone which the first introduced always does; but if it were removed, a substitute of the same caliber would not take a firm grip. There must, therefore, be ready larger calibers of every length screw in the collection. Substitutions are rare but they are sometimes necessary. We cannot recall a case in which the desired length and caliber were not ready when needed. But the preparation necessary to provide these various lengths and calibers is always an anxious task.

*Cleansing and Draping of Field of Operation.* Since we had no knowledge that such an operation had ever been done through a cast opening, protection from infection of the wound became a major responsibility. The following technic was devised and has been used in every case:

The surgeon gowned and gloved as for any sterile operation, grasps a sterile gauze pad, wet with ether, by a sterile forceps as long as available. While standing far enough away from the patient and operating table to protect his sterile gown and

gloves from contact, he thoroughly rubs the exposed skin with ether after which he discards the forceps. By carefully holding a sterile towel in front of him by its upper edge with one hand, he raises it above, free of the cast opening. At the same time he grasps the surface of the towel toward him with another long forceps near the free end, about two inches or less above its lower border. He pushes the same end under the upper edge of the cast opening at its corresponding end, without permitting the forceps or the surface of the towel to become infected. In this way he continues to tuck the successive portions of the towel edge under the continuing cast edge as far as it will reach. Then the opposite side of the towel is laid on the underlying cast surface. This portion of the skin is thus protected from infection. Taking hold of another sterile towel in the same manner, he pushes its free end under the end of the first towel and cast margin. He continues the tucking of it under the cast margin until the exposed skin surface is completely isolated from the underlying unclean cast.

The exposed skin is next swabbed with tincture of iodine followed by alcohol. After this the large sterile sheets are laid over the patient and table, the margins being pushed under the cast margin of the opening where they correspond to it and the previously laid sterile towels. (Fig. 1.) The crowding of sheet and towel under the cast may require force but it adds to the protection of the exposed skin. The manipulation of the first laid towels requires some care and skill but has been done in all of our cases without infection of the wound in any case. It is justified by the results of the operation.

*Operation.* The surgeon now palpates the great trochanter around which the opening in the cast was made and finds it about in the center. He makes a longitudinal incision five or six inches long over it, from its upper palpable margin downward through the skin and subcutaneous tissue. Sterile towels are then clamped to the margins of the incision, further protecting

the wound from infection. The incision is deepened to the bone in its whole length and particularly below the lower prominent margin of the trochanter, which is the most valuable landmark for directing the screw. The bone here is cleared in an area a few inches in all directions. The screws are to be introduced, the first about a half inch below this prominent margin, the second below the first far enough to prevent the large head from overlapping any part of the head of the first screw. This overlapping would prevent the removal of the first if necessary, without removing the second. The x-ray taken during the operation might show either or both in faulty position. Proper spacing between them would permit either to be removed without disturbing the other.

*Placing of Screws.* All that remains to be done is to place the screw properly, close the wound and apply the dressings. But the operation is to place the screw without exposing the fragments, the avoidance of which justifies all of the details and care necessary for doing it safely and effectively. But we have little or no concern about this phase of the operation. We are concerned only with the difficulty of making the technic simple and safe to others.

With the femur in forced internal rotation in the Whitman abduction cast, its neck is almost if not quite in the horizontal plane. With good retraction of the wound, one can hardly get a good view of the femur immediately below the trochanter, where the screw is to be introduced. But one can readily locate the surface of the trochanter with his fingers, the hollow space below it indicating the beginning of the shaft of the femur. He can push his finger anteriorly close to the trochanter and recognize the beginning of the neck, which will aid in directing the screw along the neck. By straining I have felt the head of the femur but do not think it necessary for safe introduction of the screw. This finger exploration for the beginning of the neck from the trochanter was not used in the

early cases but was continued after trying it. It was found safe and helpful.

Here begin the details and difficulties of

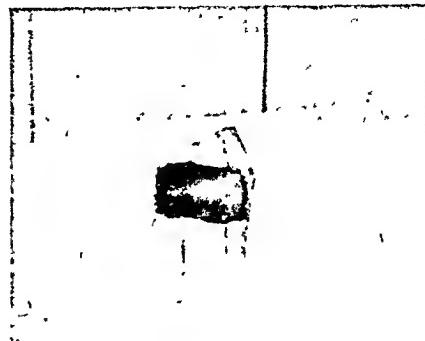


FIG. 1. The hole cut in the cast is here shown draped and ready for the making of the incision and introduction of the screws.

placing the screw, which have been justified by the results. With the femur in forced internal rotation in the Whitman cast, we know that the neck is almost if not exactly in the horizontal plane. With strong retraction of the wound margins, the point of the selected screw is placed against the outer surface of the femur, about a half inch below the easily located lower margin of the trochanter. With the x-ray film of the reduced and abducted fragments and the surrounding skeleton in the Whitman cast favorably placed in full view for guidance, and with the left forefinger lying on the neck in the channel previously made by the finger, the angle of the neck with the shaft of the femur and the trochanter can be readily plotted in the mind. Then it should not be difficult to direct the screw safely to its destination.

After the left forefinger has determined the direction of the neck, it is removed and used with the thumb to place the point of the screw in position at its selected site of entrance below the trochanter and to hold it there, directed as well as possible in the line of the neck. It is then started on its course by a metal hammer in the right hand, far enough to be held and directed by the left hand more easily. After this it is forced inward by a large screw driver while the left forefinger is again placed on the

neck in the channel previously made, the effort being to keep the course of the screw as nearly as possible in the desired direction through both fragments. A second similar screw is usually introduced in the same direction, far enough below the first one to avoid contact with it and particularly to prevent the head of the second from overlapping the head of the first, which would prevent the removal of the first for any reason without the other.

Formerly, this concluded the operation, except to close the wound and apply the dressings. But an *x*-ray was taken on the following day. If one screw or both were not satisfactorily placed, the wound was reopened and the position of the screw was changed. But it was decided to try covering the wound with sterile towels and the whole table and the patient with sterile sheets before closing it for the immediate taking of an *x*-ray. This practice has been continued since. If the positions of the screws are shown to be satisfactory by the *x*-ray, the protecting covering sheets and towels are removed. The gowns and gloves are renewed by the surgeons and the operation concluded. Both screws are then forced in as far as possible for better approximation and fixation of the fragments. The wound surface is swabbed with a 2 per cent tincture of iodine followed by alcohol. The wound is closed by a continuous chromic catgut suture of the divided tensor vagina femoris muscle, its aponeurotic expansion, and interrupted silk sutures of the skin. Sterile gauze moist with alcohol is applied to the wound, with additional dry gauze sufficient to fill the cast opening somewhat higher than the cast surface. This permits firm compression of the wound by enough adhesive plaster strips, long enough to secure this compression and prevent movement of the dressings afterward.

*Associated Problems.* Infection has not been a problem because we have had none. Nor is nonunion a problem, except that in one case after two years union was considered still absent. This case will be reconsidered later.

*Excess Length and Deviation of Screws.* We have no knowledge that this problem has arisen in connection with the use of any specially devised screws, those most commonly employed being connected with the fixation of fractures by plates and screws, which are usually all made of the same length for each method as for the Lane and Sherman plates. But the screws used in intracapsular fractures of the neck of the femur may not be made of one length, for the length necessary will vary with the individual case. A screw of uniform length, whatever the length selected, would frequently if not usually go too far in or not far enough. The screw must go through the distal or outer fragment but must not go through the proximal or head fragment, except just far enough to take a firm hold of it without encroachment on the articulation. Since the length of each fragment varies and their combined length varies or may vary in each case, it would be impossible to be sure of having ready any specially made screw of the right length when needed in the operation. Only the common carpenter screw can be used successfully and has been by us without exception for this method of screw fixation of this fracture. It would be necessary to abandon this method without it.

In a few cases when one screw was well placed and the other not, the former was retained and the latter removed. But as experience increased, the tendency grew to reintroduce the screw in better position. If it were too long and its direction good, a shorter screw of larger caliber was substituted to insure a firm grip on the bone. A loose screw or nail is always dreaded in any fracture.

#### CASE REPORTS

*Complete Failure of Screw Fixation from Faulty Use of Whitman Abduction Cast.* From the following case developed the conviction that there is an inherent weakness in the Whitman abduction treatment for intracapsular fractures of the neck of

the femur, which we had not previously suspected:

The patient, a middle-aged man, was admitted to another hospital with this type of fracture. A Whitman abduction cast was applied, according to his family physician. The patient reported that it was removed after seven weeks and then he was sent home. His physician was called because of pain in the affected joint and soon afterward had the patient admitted to the Northeastern Hospital, where an x-ray showed an intracapsular fracture of the neck of the femur with the usual typical deformity. Suspecting a refracture because of imperfect union and too early adduction of the limb after seven weeks immobilization in abduction, he was again put in a Whitman abduction cast and another x-ray taken, which showed an almost perfect reduction.

It was assumed that such a reduction could not have been accomplished if the head fragment had not become so adherent in the acetabulum, during the seven weeks' immobilization in abduction, that it could not be turned with the main or shaft fragment when it was brought to the adducted position. This would explain why, when the limb was brought back to the abducted position and a cast applied, the freshly fractured surface came into perfect reduction again. Two screws were now well introduced through the usual opening in the cast. There was no disturbance in the healing, the cast being removed after nine weeks. This was considered sufficient immobilization with screw fixation of the fragments. Since no disturbance in the rotation of the head had been suspected in patients so operated upon previously, none was expected in this case. The screws were relied on to turn the head. The patient was soon afterward sent home to remain in bed and be cared for by his physician, since it was thought that the screws could be depended upon to turn the head into adduction as usual. But the patient continued to complain of pain in the affected hip. Sometime later his physician reported that a sinus developed. The patient declined to return to the hospital and no further treatment of the fracture was attempted.

No such disturbance occurred in any previous or later cases. Firm union and good but not perfect function occurred in

every other case. But in most of them there was some limp. In probably every case an almost if not complete perfect reduction of the deformity was accomplished by the Whitman cast. But also in probably every case up to this period and for some time afterward, the normal angle of the neck with the shaft of the femur was gradually converted into a varying degree of coxa vara, i.e., an approximation to a right angle, which was assumed to be responsible for the varying degree of lameness. It had been thought also that this was due to weight-bearing on a femoral neck lacking normal firmness in the union between the well nourished outer fragment and poorly nourished head fragment because of its more limited blood supply. But following the refracture in this case, the suspicion grew into a conviction that the underlying cause of the refracture and the usual coxa vara was the same, namely, that during the period of immobilization of the intracapsular fragment by the Whitman abduction cast the reparative material within the joint capsule, callus and other exudate, had "frozen" the head fragment by adhesions to the capsule and acetabulum in the abducted position. This was immobilized so firmly that after the removal of the cast and the beginning of the efforts to bring the abducted limb into adduction, the small "frozen" head fragment could not be turned without undue straining and bending at its weak union with the main or shaft fragment. We believe that the addition of firm screw fixation will add enough support to turn the head fragment after eight or nine weeks' immobilization in abduction; but not without some bending of the neck, which is a big improvement on the non-union which the screw fixation has overcome in almost all of our cases in which it has been employed.

But in this case the intracapsular fragment had remained in continuous immobilization in full abduction for some sixteen or seventeen weeks, when the adhesions had become so firm that the screws could not turn the head into adduction but cut their

way through the bone in their efforts to do so. Thus they caused the necrosis and sinus formation. This was not due to infection.

of the screws had penetrated the acetabulum slightly. It could not be removed for a long time because the patient delayed giving consent.



FIG. 2 Postoperative refracture of neck and both screws 1, original deformity; 2, after first screw fixation; 3, after refracture, 4, three years after second screw fixation showing firm union, retained broken screws and new larger screw

As a result of these considerations in later cases the cast was removed in about ten days after operation. The skin sutures were also removed, the limb being adducted before the adhesions could offer serious resistance and a new cast applied in adduction. This case completely ended our reliance on the Whitman abduction cast alone for obtaining satisfactory bony union for weight-bearing. But it is essential for our method of screw fixation.

*Refracture of Neck with Two Screws.* For the first introduction, November 26, 1932, in a very strong, young, laboring man the screws were permitted to project from the bone more than usual because in the preceding similar case one

When removed the head of the screw was exposed with difficulty because it was covered by what appeared to be a callus formation. The heads of both screws in this refracture case were permitted to project from the bone more than usual to provide against such a difficulty. But the projection of the screws resulted in failure to bring the fragments together firmly. (Fig. 2, Part 2.) The forcing-in of the screws as far as possible had always been done previously and has been done in all cases since. In this 1932 case it was then believed that callus would fill the gap between the fragments resulting from failure to force the screws in, and that firm union would be brought about after a sufficient period. The patient was later included in a group of five similar cases in which moving pictures were taken. It proved

in his case to be a satisfactory functional result until eight months and eighteen days after the accident without interruption. He was then considered to have the best result even though he had been back at his old hard-working occupation.

After the usual period necessary for sufficient recovery of function, he had returned to his previous occupation and had reported no disturbance until readmitted to the hospital August 13, 1933, eight months and eighteen days after the accident, with an injury to the same hip region from a fall at his work. The x-ray showed a refracture at the old site with both screws broken. (Fig. 2, Part 3.) A Whitman abduction cast was applied and a new x-ray showed the fragments returned to their normal positions. Another incision was made through a hole in this new cast and the only removable portions of both screws, those external to the fracture line, were removed. A new stronger screw was substituted, its pointed end being turned away from the retained portions of the old screws, which could not be removed. There was no disturbance of the wound afterward and after the usual period the cast was removed. The patient was advised not to return to work for a prolonged period. But he did not return for advice before going back to work until asked to do so for the taking of another x-ray picture, October, 1936. (Fig. 2, Part 4.)

The decision to introduce another screw in the femoral neck fracture was reached for the following reasons: If this had not been done, the patient would have been very seriously crippled for life. If infection had resulted from the operation, he would probably have been more seriously crippled; but infection had not developed in any preceding case. It may be added it has not occurred in any succeeding case, and there was no more reason for fearing it in this than in the first operation.

This case epitomises our objections to the use of a nail or bone peg. As soon as the first screw entered the deep fragment, it tended to push it away from the other. But in the second operation a larger screw had the same effect until after its expanded head encountered the resistance of the external surface of the trochanter, after

which the continued forcing inward of the screw pulled the deep fragment toward the outer one. The deeper the screw was driven, the more firmly the fragments were pressed together, a very important factor in finally assuring bony union. A nail would be more likely to separate the fragments and less likely to compress the fragment surfaces together. Nor can we agree with those who rely on screw or nail fixation without additional fixation from a plaster cast or traction. The poor blood supply to the small head fragment, coming only through the ligamentum teres with faulty or no fragment immobilization, undoubtedly accounts for the so-called partial or total necrosis found in heads removed from old ununited fractures of the femoral neck. It has not developed in any of our cases. A nail or even a screw would tend to become loose if nothing is done to prevent movement of the hip joint; and if the screw or nail became loose, union of the fragments could hardly be expected. Firm bony union resulted in all of our cases with screws except in the refracture without screws, in this fracture with screws following the first operation, and in the next case referred to and shown in Figure 3, Part 5.

*Nonunion Two Years after Screw Fixation.* From a severe fall a strong middle-aged woman sustained an intracapsular fracture of the femoral neck with the most severe typical displacement of the fragments that I have seen. (Fig. 3, Part 1.) It is my first screw fixation of these fractures in which union failed completely. An insurance company consulted a bone surgeon who advised an extensive operation. Because it was my first failure and because in my first four screw fixations the accident had occurred from four weeks to four months before operation, I advised a second trial of screw fixation, which I did about two years after the accident. The result is shown best in Figure 3, Part 5. The roentgenologist says there is still no union with which opinion I agree.

I shall attempt an explanation of the nonunion, which is not easily accomplished. These intracapsular fractures are trans-

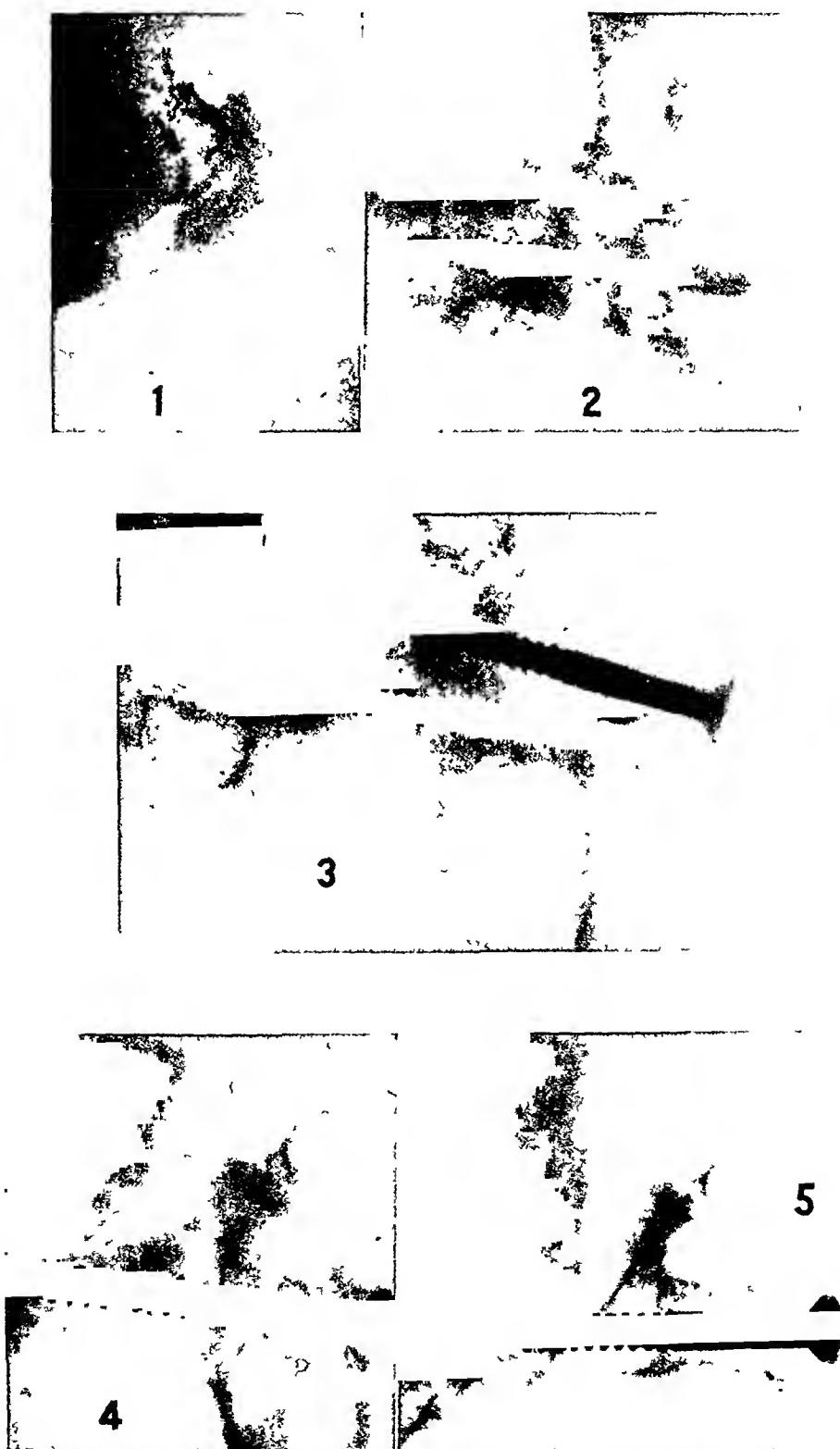


FIG. 3. Permanent nonunion after two screw fixations 1, severe original deformity, 2, after reduction and first screw fixation; 3, before second screw fixation two years after first; 4, after second screw fixation, 5, permanent nonunion.

verse fractures of the neck, the angle of which with the shaft makes the fracture line almost correspond with the line of weight-bearing. The degree of displacement usually varies from a mild upward one of the lower fragment on the upper or head fragment, as in most cases, to an almost complete absence of end-on approximation, as in this case. This displacement is probably responsible for the failure of close approximation by the Whitman abduction cast, seen in Figure 3, Part 2, after operation, and Part 3 taken about two years after the operation. The case as shown in this figure and the preceding case with refracture and broken screws are the only ones showing so poor an approximation. It is my present opinion that this was the cause of the trouble in both, and that the refracture patient had walked on an ununited fracture until the refracture occurred so many months after the operation. This assumes that he walked and worked on the fragments supported by the screws until the refracture, which nonunion we have suspected for a long time but have been unwilling to assert until this case seemed to support the suggestion. However, there may have been some union.

The woman has used crutches since her cast was removed about three months after the operation, suggesting that union had never developed, a failure which did not occur in any other cases. Permission to begin weight-bearing was long delayed after the second screw introduction and the increase in weight-bearing was very slow. Figure 3, Parts 4 and 5 show the successive x-rays taken since. The most interesting development was that notwithstanding the x-ray evidence of nonunion, the weight-bearing ability increased. The patient walks about the home without crutches and with only a cane goes out on the street. It is difficult to decide what course to pursue. We know that a distinct weight-bearing ability can be present in the absence of bone union. We have no knowledge that any of the extensive operations done in these late stages produce better results. If pain becomes more troublesome, I would be inclined to advise removal of the screw and permit the trochanter fragment to develop support from the condensation of the surrounding connective tissue and the untorn joint ligaments. It has done this very successfully in many of these ununited fractures. It is in condition to do this successfully in this case after three years of nonunion in a very favorable position. The patient up to the present time is very well satisfied with her condition.



# CHEMOTHERAPY IN OSTEOMYELITIS

ABRAHAM O. WILENSKY, M.D.

NEW YORK, NEW YORK

THE cumulative experience discussed in this communication is based upon that recorded previously in the literature, upon experiences related to me by other surgeons and pediatricians and lastly upon my own personal experiences. The material is composed of the ordinary run of cases of acute inflammation of the bones of bacterial origin (acute osteomyelitis); and no case of tuberculous or luetic infection is included. Chronic osteomyelitis is included only when recrudescences or exacerbations of infection bring it within the classification of an "acute" case.

The ordinary acute hematogenous cases are commonly due to infection by the *Staphylococcus aureus*. Extension cases of the skull following nasal accessory sinus infection are more commonly due to streptococci of the hemolytic and nonhemolytic groups. Extension cases following otological infection are due to streptococci and pneumococci most commonly. Primary cases of osteomyelitis, wherever they occur, are due to a variety of organisms depending upon environmental and causal conditions; commonly they belong to the colon groups; and in military wounds they form the commonest cause as a fecal infection due to the unnatural conditions of army life in the field. In considering the effects of chemotherapy with the new drugs of the sulfanilamide group, the bacteriology should be kept in mind as the various drugs exhibit different potencies with the various classes of bacteria.

The drugs of the sulfanomide group: sulfanilamide, sulfapyridine, sulfathiazole, sodium sulfapyridine, etc., can be administered by mouth, by hypodermic injection and by continuous subcutaneous and intravenous infusion. They can also be instilled locally into a wound, dissolved in plasma and reinjected into the circulation,

and injected into the subdural cerebrospinal space by lumbar puncture. They can be combined with other drugs as arsphenamine or heparin, with antibacterial gas sera, with radiation therapy and with blood transfusions. Each of the drugs seems to have a special affinity for a different group or strain of bacteria. The drugs are rapidly absorbed and quickly excreted so that the dosage must be fairly large and frequently administered. They do not interfere with certain physiological functions such as blood groupings, with normal antibacterial activities and with bacteriophage action. When carefully administered and checked by repeated laboratory examinations the drugs are safe to administer and gastrointestinal and/or hematological complications can be entirely avoided or markedly ameliorated.

There is no absolute agreement as to which of the drugs is best except that sulfapyridine seems to work best with pneumococcal infections. At the present writing sulfathiazole seems to be in greatest favor for staphylococcal infections. My own experience is that all things considered, sulfanilamide works best in the general run of surgical infections, and in the latter type of case, none of the others has seemed superior. Apparently it is the custom to change from one to the other drug if no satisfactory results are quickly obtained; but in two severe cases of my own in which this method was tried, no perceptible difference was noted. Some of the observers put greater reliance on sulfathiazole. Sulfomethylthiazole shows too many toxic manifestations; but in a personal case in which this was tried after the others, no superior effect was noted. Azisulfamide is advised by Horan and French<sup>7</sup> when maximal concentration is desired in minimal time. Sodium sulfapyridine is advised

by the intravenous route for a similar reason, but in one personal case in which this was employed no effect was noted.

The drugs of the sulfanilamide group act in the animal body very much like they do in the test tube. For the necessary effect an intimate contact is necessary between the bacteria and the drug and this takes place either exclusively or to the maximum effect in the circulating body fluids—the blood, the lymph and fluids contained in or circulating in various hollow spaces (i.e., peritoneum, pleura, meninges, etc.). The effect is a bacteriostatic one and bacterial activity and growth are only inhibited. Destruction of the bacteria is facilitated and occurs during this dormant state by the natural antibacterial agencies in the body and the latter are more efficient after bacteriostasis is accomplished and while bacteriostasis is present. Therefore, drugs must be administered for a sufficient length of time and in sufficient concentration to enable them to work adequately; otherwise bacterial activity is not inhibited, the bacteria are not destroyed and the pathological condition increases. For this reason, recurrences occur frequently in clinical practice.

There is no complete agreement as to the best method of administration of these drugs. The main index of the sufficiency of the chemotherapeutic agent is the concentration in the blood; and, in order to make certain of this, blood determinations are necessary. Since the therapeutic aim is to attain a concentration in the blood of 10 to 15 mg. per 100 cc. as rapidly as possible, all available routes of administration should be attempted, by mouth, by hypodermoclysis and by the intravenous and intramuscular routes. Intrathecal administration is superfluous because it was noted by Marshall<sup>11</sup> that the concentration in the cerebrospinal fluid is close to the concentration in the blood. Not all patients of the same weight respond similarly to identical dosage, and one should, therefore, vary the dosage with different patients according to the concentration attained in the blood.

Infants will tolerate the drug well, the dose being from one-third to one-half of the adult dose, while children require from one-half to three-fourths of the adult dose.

#### CLINICAL EXPERIENCE

*In Acute Primary Osteomyelitis.* The prophylactic use of the drugs of the sulfanamide group seem especially indicated in all civil accidental and operative bone wounds and in all bone wounds suffered in war in which infection might be expected to take root and flourish. This should not relieve one of the responsibility of employing all of the usual and well tried procedures (i.e., cleansing, débridement, etc., in all traumatic wounds (civil and military) and aseptic technic in all operative wounds) to which we have become inured by many years of successful usage. In spite of the fact that previously these measures have attained a high percentage of success, the helpful action of these drugs should be added in all suitable cases.

The latest preparations are in powder form and the powder may be insufflated directly into the wounds. In the general run of wounds sulfanilamide powder has served me excellently and I shall continue to use it prophylactically. Recently, sulfaguanidine has been proposed in cases in which the intestinal canal has been opened: the drug is not easily or readily absorbed but, nevertheless, exerts a continuous inhibitory effect upon the organisms inhabiting the intestinal tract with which it is placed in intimate contact. For the latter reason it is also recommended that the drug be given by mouth. In military wounds (battle wounds, bombing raid wounds, etc.), of the pelvis or lumbar spine in which the bowel is also opened, sulfaguanidine might be advantageously used as indicated.

*In Acute Hematogenous Osteomyelitis with Especial Reference to the Long Bones.* In order to understand the availability for and the therapeutic effectiveness of chemotherapy in acute osteomyelitis of the hematogenous variety, one should remember that the latter consists pathologically

and clinically of two distinct phases: (1) the initial phase of the general infection (i.e., with bacteriemia), and (2) the phase of development and progression of the local bone lesion.

(a) *Effect of Chemotherapy during the Stage of General Infection (Bacteriemia).*

The available information corroborates the experimental work and makes clear that chemotherapy is therapeutically most active only during the phase of bacteriemia, when intimate contact can be established between the drug and the bacteria in the circulating blood; and that the effectiveness of action is directly proportional to the capabilities for and the thoroughness with which this intimacy can be accomplished.

When the proper member of the sulfanamide group is employed, and a sufficient concentration of the drug is established in the circulating blood for a sufficiently long time, the cumulative experience indicates that the general infection (i.e., bacteriemia) can, in the majority of the cases be eliminated fairly promptly. When this effect is obtained, that part of the clinical picture, which is caused by the presence of living bacteria in the blood stream (i.e., chills, at least part of the fever, toxicity, etc.), is either materially lessened or entirely eliminated in direct proportion to the effectiveness of the bacteriostatic action produced by the drug. In effect, this leads to an amelioration of the general clinical symptomatology; but this should not delude the clinician into believing that an equal effect is necessarily being produced in any existing local bone lesion *pari passu* with the general improvement.

Chemotherapy is not always capable of controlling the bacteriemia because the rate of production and discharge of the bacteria into the general blood stream is sometimes larger than their chemical inhibition and later destruction. This is not always due to the failure to produce the proper concentration of the drug in the blood stream; but, at the present writing, it seems most probable that it is due to the failure to make use of the drug sufficiently

early. Widespread distribution of metastatic lesions in the visceral organs, musculature, etc., as well as in the skeletal system, may have preceded the exhibition of the chemotherapy and determine the persistence of any bacteriemia and the subsequent final fatal result.

(b) *Effect of Chemotherapy on the Local Bone Lesion.* Should a beneficent therapeutic effect on the general infection result from the chemotherapy, one is then left with one or more local bone foci. The local focus is a consequence of a local thromboembolus, the main characteristic of which is an exclusion of the sequestered portion of the bone from the general circulation.

Any bacteria present at these foci are locked away within the interior of the embolic area. Any intimacy of contact between the drug and bacteria is usually impossible because of the plugging effect of the thrombo-embolus. Theoretically, under such conditions, chemotherapy should yield no, or minimal beneficent therapeutic effects. Furthermore, bacteria could continue to grow within the thrombophlebitic area and could bring about various local complications, i.e., an infection in a joint. Then, too, if part of such an infected clot should break off or become dislodged to travel to and become blocked in a distant part of the body, metastatic lesions could occur and develop in spite of the saturation of the body with the chemotherapeutic drug.

Cumulative experience, including my own, indicates the entire agreement of clinicians with these theoretical considerations. In actual practice, chemotherapy is a failure as far as the local lesion is concerned for the above reasons and, above all, because the progression of the local bone focus is due to physical causes, i.e., the deprivation of a sequestered area of its normal blood supply. While the general toxic symptoms may show a variable degree of amelioration, as indicated previously, the temperature may, nevertheless, continue as a reflection of local inflammatory conditions and activity and not

because of any general infection (bacteremia). The local lesion usually proceeds to further development (necrosis and sequestration) and even to the production of its usual complications (e.g., an adjoining joint infection—brain abscess or meningitis from a cranial osteomyelitis—sinus thrombosis from a mastoid) which can lead to a fatal issue.

If the growth of any bacteria, excluded at first from contact with the general circulation because of its position in the thrombophlebitic area, should later succeed in forming contact with freely circulating blood, such an active thrombophlebitic process may continue the general infection (positive blood culture) by continuing to shed bacteria into the general peripheral circulation. In actual practice chemotherapy has no sterilizing effect under such conditions and, in order to sterilize the blood, it is necessary to eliminate by excision the offending segment of blood vessel which contains the infected thrombus.

There is almost laboratory proof of this statement in the clinical history of the following case:

In a boy of twelve an acute hematogenous osteomyelitis of the tibia of severe grade developed; and, although the general signs of intoxication were ameliorated by sulfathiazole, a positive blood culture persisted equal to ten to fifteen colonies of bacteria to the cc. of blood cultivated. Then a thrombophlebitis of the associated saphenous vein was recognized; and, when the latter vein was excised, the blood became sterile and the boy made a complete recovery.

Sometimes excision of the active thrombophlebitic lesion is not possible because of its inaccessibility as in the anatomically related veins of the spine, the pelvis or the base of the skull. And the situations of deeply placed thrombophlebitic veins in the interior of the long bones, or in the extreme depths of their covering musculature are not always discoverable. Under such handicaps, chemotherapy has been mostly a failure clinically, even though an

unprecedented brilliant unexplainable cure results rarely.

(c) *Effect in Chronic Osteomyelitis.*

Chronic osteomyelitis is a continuation of the local lesion phase of acute osteomyelitis, usually of the hematogenous variety. Similar therapeutic results occur in any long standing ("chronic") case, during any period in which any recrudescence and exacerbation of infection, either locally, or generally, is accompanied by a demonstrable bacteremia.

Anything which has been previously said regarding the treatment of the local bone focus in the acute stage applies with equal force in the long drawn out chronic stage. In making any deductions regarding the effects of chemotherapy in the chronic stage, one must make allowances for those disabling mechanical conditions, i.e., foreign bodies, sequestra, which prevent closure of the bone wound and its sinuses.

If the local focus harbors an open wound, some therapeutic effect of chemotherapy might be obtained by the local application of the drug in the wound. This, however, would be a purely surface phenomenon and would not influence the progression of the deep pathological condition.

*In Extension Osteomyelitis.* Extension osteomyelitis is most commonly found in the skull and is intimately bound up with nasal accessory sinusitis and with otogenous infections. All of the discussions must necessarily take into account the prophylactic effect of chemotherapy in these preceding infections: the effect in the treatment of the osteomyelitis itself; prophylactically in the prevention of the intracranial complications which so frequently occur; and therapeutically in the treatment of the latter.

*In Extension Osteomyelitis of the Skull Following Accessory Nasal Sinus Disease.* In the early stages of infection and in mild cases strictly limited in scope to the nasal accessory sinuses, chemotherapy seems to be unnecessary inasmuch as most of these cases undergo spontaneous resolution and cure. In the cases of severe infection of the

nasal accessory sinuses with high fever, chemotherapy seems to act favorably in bringing down the fever (Kramer;<sup>8</sup> Kulkin<sup>9</sup>); but Kramer<sup>8</sup> remarks that "the discomfort associated with the administration" of the drug "outweighs in most cases the benefits attained by the reduction in the temperature." In this regard it seems true that the indiscriminate use of the drugs of the sulfanamide group should be deprecated and certainly its use by the general public without adequate medical supervision should be restricted.

There is no prophylactic effect as far as the occurrence of any complicating osteomyelitis, and in any event the course of the infection should be carefully watched and controlled, because of the tendency of the drug to mask the spread of the disease into the cranial bones.

During the early stages of the development of any osteomyelitis of the cranial bones, chemotherapy seems to have a somewhat favorable effect upon the general clinical manifestations of fever, etc., even while the bone lesion is advancing. Otherwise, the following varied experience is available: the effectiveness of chemotherapy was doubtful because it was necessary immediately to combine with it surgical methods (Furstenberg);<sup>5</sup> at the University of Illinois the experience was frankly disappointing (Fabricant);<sup>4</sup> at the Mayo Clinic chemotherapy was "quite effective in the early stages of the disease" (i.e., osteomyelitis) but of little or no value once sequestration has taken place (Adson);<sup>1</sup> chemotherapy was fruitless in the treatment of an established osteomyelitis (Kramer);<sup>8</sup> chemotherapy was dangerous because of an undue reliance which might be put on the drug to the exclusion of the necessary surgery (Mosher);<sup>13</sup> and that in all cases the administration of these drugs has tended to obscure the further development of the clinical and pathological picture and the development of dangerous complications. My own experience parallels this in every way; chemotherapy has not prevented the occurrence of

osteomyelitis of the cranial bones; chemotherapy tended to mask the development and spread of the infection into the cranial bones; once established it has had no effect upon the osteomyelitis and surgical eradication of the disease was necessary.

The only contrary belief is that of Champ Lyons,<sup>10</sup> of the Massachusetts General Hospital, who reports good results from the use of chemotherapy in cranial osteomyelitis.

*In Extension Osteomyelitis of the Skull Following Middle Ear and Mastoid Infection.* Osteomyelitis of the mastoid, the petrous, and the squamous portions of the temporal bone occurs as a spread by contiguity from an infection of the lining membrane of the middle ear and associated cells of the mastoid.

Pediatricians report favorable prophylactic results from the use of chemotherapy in early cases of otitis media; but, in these early cases, favorable results are quite common without the use of chemotherapy. And great caution and careful observation are necessary in these early cases for fear of the drug masking the developing clinical picture and the spread of the infection into the bone.

Bowers'<sup>2</sup> results would indicate that when the drug is given early before bone softening has occurred, operation is decreased by half. Late treatment doubled the operative indication as compared with those treated early and adequately. In the experience of Horan and French<sup>7</sup> the incidence of mastoiditis was only 3.4 per cent, compared with 22.7 per cent before the introduction of sulfanilamide therapy. The experience is further corroborated by Hebble.<sup>6</sup>

The clinical experience with sulfanilamide at the Massachusetts Eye and Ear Infirmary has led Converse<sup>3</sup> to the belief that chemotherapy should not be routinely used as an adjunct to the usual measures for the treatment of infections of minor severity because: (1) Premature initiation of the drug therapy has made complete clinical evaluation of the patient difficult,

and progress of the infection to a complicating endophlebitis has been obscured during treatment, (2) There has been recurrence and further spread of the infection after omission of sulfanilamide in patients who had clinically appeared to be healed. (3) The danger of toxic manifestations necessitates the hospitalization of all patients receiving the drug.

*Chemotherapy in the Intracranial Complications of Osteomyelitis of the Skull.* According to Kramer<sup>8</sup> in rhinological cases, "the complications due to lymphatic and vascular involvement, with and without meningitis, have responded amazingly to the sulfanomid group. For the first time in rhinology recoveries have been obtained in patients with these complications." It has been "found . . . absolutely necessary, however, to attack surgically the source of the infection in order to obtain a permanent cure." At the Mayo Clinic, Adson<sup>1</sup> has also found it "of value in controlling and curing a number of patients with meningitis. It is of questionable value once a brain abscess has developed, but judging from their experience . . . it is quite effective if given in the early stages of acute encephalitis."

Maybaum<sup>12</sup> and his associates only use chemotherapy (sulfanilamide) in otitic complications—meningitis, sinus thrombosis and abscess of the brain. Removal of a bone focus or other localized pathological condition (extradural abscess) is imperative, but in the presence of extreme bacterial meningitis, intensive chemotherapy is advised for twenty-four to thirty-six hours prior to operation. In petrositis the drug is dangerous during the period of observation because of the tendency to mask the clinical picture, but once the diagnosis is made chemotherapy should be added to any operative manipulation. The drug is especially useful in continued otitic sepsis after a thorough surgical eradication of any localized foci has been done.

Chemotherapy has introduced a peculiar antagonistic effect. On the one hand chemotherapy may so mask the symptoms that an apparently symptomless meningitis may

develop; on the other hand, chemotherapy is establishing a dominating place for itself in the successful treatment of meningitis. In the twenty-five years prior to 1936, only seventy-six recoveries from streptococcic meningitis were reported in the literature; since 1936 over 200 recoveries have been reported. Mortality has dropped from 97 to 35 per cent. Success in treating intracranial complications, according to Maybaum<sup>12</sup> and his associates, only follows when the original focus has been thoroughly eradicated, because while sulfanilamide is effective in clearing body fluids of bacteria, it is not effective when the latter are locked up in osseous tissue.

In the only personal experience I have had with intracranial spread of the infection chemotherapy seemed to have no effect. Sulfanilamide, neoprontosil, sulfathiazole, and sodium sulfapyridine were used, by mouth, hypodermically, by continuous subcutaneous infusion and by the intravenous route.

Latency of symptoms is further corroborated and commented upon by all observers (Converse,<sup>3</sup> Bowers,<sup>2</sup> Maybaum,<sup>12</sup> et al., Smith and Coon,<sup>14</sup> Hebble,<sup>6</sup> etc.). The apparently too early interruption of chemotherapy has been followed by unheralded intracranial complications after a period in which there was apparent more or less complete cessation of symptoms. An obligation is therefore created to continue sulfanilamide therapy, if once begun, until there is bacteriologic as well as clinical evidence of complete subsidence of the infection. Premature cessation of chemotherapy on clinical evidence alone permits exacerbations and recrudescences of infection in patients with ill prepared defensive mechanism.

*Chemotherapy in Dento-alveolar Infections.* Only a few oral surgeons and dentists are ready to make definite statements regarding the use of chemotherapy in dento-alveolar infections and their complications. The consensus of opinion seems to be that chemotherapy does not prevent the spread of infection from a purely dental

lesion into the substance of the jaw bone, nor the further progression of any resulting osteomyelitis or of its complications.

#### COMMENT

In actual practice, in the treatment of osteomyelitis, chemotherapy with the drugs of the sulfanamide group has not produced the consistently startling results which it has had in some medical conditions, notably the pneumonias. The observed results have varied all the way from the absolutely negative to occasional very satisfactory effects; they have been relatively good in the phase of general infection (bacteremia), and relatively without effect and sometimes dangerous as far as the local bone focus of osteomyelitis was concerned.

The results of chemotherapy are not always predictable owing to the various obstacles, enumerated in this communication, to the efficient exercise of the bacteriostatic power of the drug, to the occasional difficulty of maintaining the proper concentration of the drug, to the necessity of matching the proper drug to the provocative organism, to the occurrence of certain toxic effects of the drugs themselves, and to the difficulty inherent in removing inaccessible foci of infection by surgical means. Chemotherapy has not prevented the spread of pathological conditions or the occurrence of complications, and in general surgical practice and especially in osteomyelitis have not been as satisfactory as one would wish. Sometimes the proper interpretation of good results is difficult owing to the possibility that such beneficent results have occurred spontaneously as they have done many times in the past before this form of chemotherapy was available.

Beneficent retrogressive changes are commonly seen and are common clinical knowledge in the clinical histories of many cases of acute osteomyelitis which in past years and before the advent of the new

chemotherapeutic drugs have come under the care of all surgeons. Sometimes the beneficent improvements in the various aspects of the clinical, anatomical and pathological pictures attained remarkable extents and were most gratifyingly surprising when just the opposite outcome seemed imminent. Such unaided spontaneous outcomes undoubtedly are occurring today and will continue to happen.

In the new experience with chemotherapy such results also appear and it remains to be seen in the accumulated experience whether the actual and percentage relationships will be different or approximately the same. In any event in making any conclusions as regards the action of any of the new chemotherapeutic drugs in osteomyelitis the possibilities for spontaneous, unaided recovery should be remembered.

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# TREATMENT OF LYMPHOGRANULOMATOUS STRICTURES OF THE RECTUM WITH SHORT WAVE DIATHERMY\*

RICHARD T. SHACKELFORD, M.D. AND J. ARTHUR WEINBERG, M.D.

Assistant Visiting Surgeon, Johns Hopkins Hospital  
BALTIMORE, MARYLAND

Assistant Visiting Surgeon, Johns Hopkins Hospital

FOR many years patients with stricture of the rectum due to lymphogranuloma venereum have been returning to the rectal dispensary at the Johns Hopkins Hospital for whatever treatment was then in vogue. In 1940, Martz and Foote reported three men and two women with this disease whom they had treated with diathermy combined with Frei antigen inoculations. They obtained apparent cure in all five of these cases. Such an encouraging report led us to attempt our own evaluation of the method.

Lymphogranuloma venereum is a specific disease produced by a filtrable virus which is usually transmitted by sexual intercourse. The initial lesion is a small painless herpetiform or papular nodule which usually lasts only a few days and is unnoticed or disregarded by the patient. The secondary manifestations vary with the sex of the individual and the site of the primary inoculation. In the male the primary lesion usually occurs on the external genitalia and drains by way of the lymphatics to the inguinal glands resulting in the formation of buboes. In the female the site of inoculation is usually the cervix or the posterior vaginal wall and drains to the rectal and perirectal lymphatics causing a proctitis and perirectal fibrosis. The proctitis progresses, ulcerates and is usually associated with a profuse bloody purulent discharge. Elephantiasis vulva, anal condylomas, and perirectal abscesses and fistulas also occur as secondary manifestations. Occasionally, rectal lesions develop in the male as a result of direct implantation in the rectal mucosa by pederasty, by spreading up the rectal mucosa from a primary lesion at the anal

margin or as an extension from a lesion on the urethral meatus to the posterior urethra which drains to the rectal and perirectal lymphatics. The tissue changes are those of a nonspecific granuloma. The diagnosis is made by the Frei test which is an allergic reaction to the intracutaneous inoculation of the sterilized extract from the exudate of a known lesion.

Almost every form of chemical, biological, radiological, electrical, surgical and physical treatment has been used without very promising results after the secondary manifestations have developed. Recent reports have offered attractive results with the use of the sulfonamides but our experiences with these have not been good when used late in the disease. We decided to treat some of our rectal strictures with diathermy alone. A short wave machine was used. A metal plate connected to one pole of the machine was applied to the lower abdomen and the other pole was connected to a Hegar dilator which was inserted into the strictured area. The largest dilator that could be inserted without causing the patient too much discomfort was used. Treatments were given from two to six times per week for a period of twenty minutes each, as much current being used as the patient could tolerate. Five patients were treated in the above manner and two patients were used as controls. In the controls similar Hegar dilators were inserted in a similar manner for periods of twenty minutes each but no diathermy was used. The following case reports show our results:

## CASE REPORTS

CASE I. L. B. (J. H. H., No. 104032), a female, forty years of age was first seen in the

of the Johns Hopkins Hospital, Baltimore, Maryland.

\* From the Departments of Surgery and Physiotherapy of the Johns Hopkins Hospital, Baltimore, Maryland.

gynecology dispensary on March 30, 1937, at which time she complained of pain on urination, dyspareunia and passage of fecal material

eight treatments, the method was stopped at which time the stricture was still palpable and that portion within reach widely patent,



FIG. 1. Case III. Before diathermy treatments.



FIG. 2. Case III. At the end of diathermy treatments.

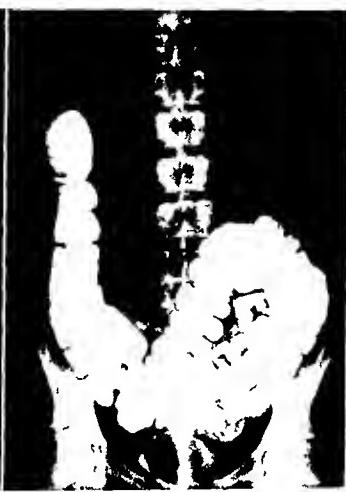


FIG. 3. Case III. Three months later.

through the vagina of two years' duration. She had been married fourteen years but had never been pregnant. Examination at that time showed elephantiasis of the right labia, condylomas acuminata about the rectum, a urethral caruncle and a fistula extending into the right buttock. A rectovaginal fistula and a dense stricture of the rectum were also present. The Frei and D'Melcos tests were negative at that time. She was admitted to the hospital April 5, 1937. Her rectal stricture was forcibly dilated under anesthesia. Following discharge from the hospital she returned to the rectal dispensary for weekly dilatations for forty-four weeks. On June 6, 1938, sulfanilamide orally was begun in addition to the weekly dilatations. This was continued for forty-one weeks with great improvement in the amount of discharge but persistence of the stricture. On September 19, 1938, the Frei test was positive and the following week, which was during the course of sodium sulfanilate therapy and weekly dilatations, the rectovaginal fistula was noted to have healed. She had had a total of ninety-eight dilatations up to this date. On May 20, 1940, the sodium sulfanilate was stopped and the patient began a series of twenty minute diathermy treatments in the physiotherapy department, three days weekly, with a No. 18, the largest size dilator. Barium enema x-ray study at that time showed a marked deformity of the rectum. On November 21, 1941, after four months of such therapy, totalling forty-

although the discharge had ceased. An x-ray at this time, however, showed no change in the deformity of the rectum when compared to that made just previous to the instigation of diathermic treatments. All therapy was then discontinued and on January 21, 1941, she returned for a check up at which time examination showed the stricture still to be present but patent; the rectovaginal fistula remained healed and the x-ray after a barium enema remained the same as on her previous examinations. On May 26, 1941, she again returned with no symptoms but her local condition unchanged.

CASE II. C. M., (J. H. H. No. 177033). This twenty-eight-year old married, colored woman was first seen in the Johns Hopkins Hospital dispensary on September 22, 1939, at which time she was found to have a pharyngitis from which she rapidly recovered. On December 13, 1939, she returned to the gynecology dispensary with the complaints of tenesmus and bloody, watery stools of one year's duration. She also stated that the menstrual periods had been irregular for the past nine months and were associated with progressively increasing dysmenorrhea. Her immediate and most urgent complaint was the presence of a painful boil on her right thigh which had appeared one week previously. Examination on December 13, 1939, revealed an abscess on the right thigh, adjacent to the labia, bilateral inguinal adenitis, a purulent vaginal discharge and an irregular, nodular mass partially obstructing the rectum.

Her Wassermann test was negative. The urine contained pus and the blood showed a moderate leucocytosis. A diagnosis of lymphogranuloma

January, 1936, she returned complaining of a rectal discharge of nine months' duration and was found to have elephantiasis of the labia,



FIG. 4. Case IV. Before diathermy treatments.



FIG. 5. Case IV. At the end of diathermy treatments.



FIG. 6. Case IV. Three months later.

venereum was made and she was started on sodium sulfanilate zii three times a day accompanied by weekly rectal dilatations. A barium enema on March 7, 1940, showed a constricted, deformed rectum with a dilated colon. On April 15, 1940, a rectovaginal fistula was found to have appeared. The sodium sulfanilate was stopped and the patient was started on physiotherapy treatments of twenty minutes each twice a week with a No. 10 dilator which was gradually increased until June 10, 1940, when a No. 18, the largest size could be inserted. This size was continued until cessation of treatment on July 19, 1940, after forty-three applications. On April 8, 1941, she was seen for a check up at which time the vesicovaginal fistula as well as the stricture were still present. An x-ray after a barium enema showed that the disease had progressed and the rectum was even more deformed than before treatment had been commenced.

CASE III. V. T. (J. H. H. No. 124871). In 1934, the patient had a full term, spontaneous delivery in this hospital and was found to have a positive Wassermann reaction. She was given antiluetic treatment during her pregnancy. Her history stated that three years previously at the time of her only other pregnancy she had been found to have syphilis and was treated for twelve months elsewhere, during which therapy she gave birth to a normal child. In 1935, she returned with an acute Bartholin's abscess which was incised and drained successfully. In

multiple fistulas-in-ano and rectal ulceration and stricture. She was admitted to the hospital on March 6, 1936, and the fistulas were excised. She was discharged from the hospital on March 12, 1936, and seen in the rectal dispensary on four subsequent occasions until April 8, 1936, when she disappeared. On February 26, 1940, she returned to the rectal dispensary because of marked constipation and discharge from the rectum. Examination then showed a tight, dense rectal stricture with almost complete obstruction, multiple fistulas-in-ano with abscess formation, condylomas lata and a rectovaginal fistula. The stricture was dilated with a Kelly clamp and she was started on sodium sulfanilate zii three times a day. She returned for dilatations twice a week and on March 15, 1940, x-ray after a barium enema showed a marked deformity of the rectum with nearly complete occlusion. On April 3, 1940, she was started on diathermy treatments five days a week beginning with a filiform dilator. The size of this was progressively increased until at the time of cessation of the therapy on October 25, 1940, after a total of eighty-four treatments a No. 17 could be inserted. An x-ray at this date showed the rectal lumen to be more patent but the deformity otherwise appeared the same. All therapy was then stopped and on February 21, 1941, she returned for a check up. At this time she had gained five pounds in weight, had few symptoms and though the stricture felt softer it was narrower than on her

previous visit. A barium enema showed both the deformity and the stricture to be more marked.

ulceration. X-rays showed the condition unchanged from the previous examination.

CASE V. C. C., (J. H. H. No. 195513), a



FIG. 7. Case vi. Before diathermy treatments.

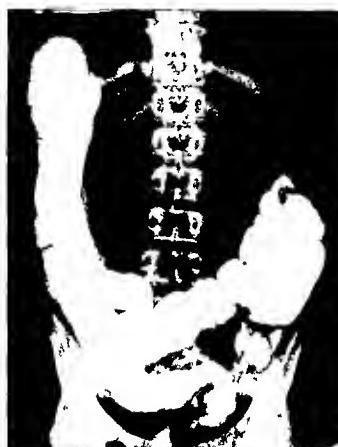


FIG. 8. Case vi. At the end of diathermy treatments.



FIG. 9. Case vi. Three months later.

CASE IV. M. S., (J. H. H. No. 163822), a colored woman, was first seen in the out-patient department of the Johns Hopkins Hospital in June, 1933, at the age of thirty-eight for difficulty in defecation. Examination showed a dense stricture of the rectum which was gradually dilated to admit a No. 8 Wales bougie and she was discharged in March, 1934. She returned to the clinic in February, 1939, complaining of rectal bleeding and constipation. Examination then showed a dense stricture beginning two and a half inches above the anal margin which admitted a Kelly clamp with difficulty. The Frei test was positive. The stricture was dilated but the patient did not return to the clinic until April 18, 1940, when her symptoms had returned. At that time the stricture admitted a No. 10 Hegar dilator. X-rays showed a deformity and stricture of the rectum extending to the rectosigmoid junction. She was given bi-weekly diathermy treatments until October 25, 1940, receiving a total of fifty-six treatments. The stricture then admitted a No. 18 Hegar dilator with ease and she was symptom free. X-rays showed some dilatation of the distal portion of the stricture but the extent of the lesion had not changed. She returned to the clinic on February 12, 1941, for a check up examination. In the interim her bowels had moved daily and she had had no bleeding. The stricture had contracted slightly and admitted a No. 16 Hegar dilator. The surface was smooth and there were no signs of

colored girl was first seen in the out-patient department of the Johns Hopkins Hospital in 1930 at the age of fifteen, complaining of a tender, swollen mass in the right groin. She denied the presence of any genital lesion and gave no history of a vaginal discharge. The mass was incised and drained and healed within three weeks. Several months later she began to have difficulty in defecation and noticed that her feces were occasionally streaked with blood, mucus and pus. She was seen in the rectal clinic and examination revealed a stricture of the rectum but she did not return for further treatment. She next came to the clinic in 1935 when she complained of abdominal pain and a profuse bloody diarrhea. She was admitted to St. Joseph's Hospital where a rectal stricture was dilated under an anesthetic and she was given intravenous tartar emetic. Her condition improved and she was discharged five months later. In March, 1940, she returned complaining of bloody diarrhea, fever, chills, nausea and vomiting. She was admitted to the Johns Hopkins Hospital on March 13, 1940. At that time rectal examination showed a dense stricture two inches above the anal margin, which admitted a Kelly clamp. Her hemoglobin was 42 per cent and the Frei test was positive. She was given two blood transfusions and her stricture was dilated. Her bowel movements decreased in number, her general condition improved and on March 27, 1940, she was started on rectal diathermy treatments. At that

time the stricture admitted a No. 8 Hegar dilator. She was discharged from the hospital on April 14, 1940, and her treatment was continued in the out-patient department. She received eighty-five treatments up to August 5, 1940, when her stricture admitted a No. 17 Hegar dilator and she was symptom free. Recent attempts to have her return for a check up examination have been unsuccessful and we know nothing about her condition since that date.

CASE VI. P. S., (J. H. H. No. 13538—Control), was first seen in the gynecology dispensary in 1909 at which time her age was given as twenty-one. She then complained of a sudden onset of chills, fever and pains in her right hypochondrium. A diagnosis of acute pelvic inflammatory disease was made and she was given hot douches of pulvis menthol compound after which she recovered satisfactorily. Her only child was then six months old. In September, 1916, she returned with an abscess of her left vulva which was incised and drained, also followed by recovery. In January, 1918, she returned with a stricture of her rectum which was dense enough to require admission to the hospital for forcible dilatation under anesthesia. After two days of hospitalization and one visit to the dispensary she did not return for further treatment. In June, 1920, she returned to the laryngological clinic complaining of a sore throat. Her Wassermann test was negative. There were no rectal complaints and there is no note as to its condition at that time. In June, 1927, she returned to the gynecology dispensary with a marked rectal stricture and hemorrhoids and was admitted to the hospital for dilatation of the stricture under anesthesia. She remained from August 4 to August 10, 1927. In March, 1929, she returned to the rectal dispensary with a rectal stricture which was dilated at varying intervals over a period of five months with a No. 6 to a No. 8 Wales bougie, a total number of six dilatations. In October, 1931, she again returned with a dense stricture, a rectovaginal fistula and arthritis. She was given a course of tartar emetic with weekly dilatations for the next three years, receiving a total of sixty-six dilatations and injections. In January, 1935, her Frei test was reported positive and she continued dilatations at intervals as the stricture continued to recur. In March, 1936, x-ray with a barium enema showed an irregular, fusiform deformity of the rectum without occlusion.

In July, 1939, she returned nearly obstructed by her stricture and weekly dilatations were again carried out. In August, 1939, the x-ray was similar to that in 1936. On June 24, 1940, she was started on five daily dilatations per week in the physiotherapy department, having the dilator in place for twenty minutes and no diathermy being used. By this means, she was increased from a No. 12 to a No. 18 Hegar dilator, the largest size. A total of eighty dilatations were used. The treatment was discontinued until October 21, 1940, at which time a barium enema showed that the stricture was dilated in its distal portion which could be reached by the dilator, but the upper portion remained the same as before. All treatment was then stopped for three months. On December 2, 1940, it was noted that the palpable part of the stricture was again becoming narrowed and on February 3, 1941, another barium enema showed that the entire stricture had resumed the same amount of constriction as before the beginning of physiotherapy. She is now returning once weekly for dilatations with a No. 6 Wales bougie.

CASE VII. M. N., (J. H. H. No. 203719—Control), a colored woman, aged thirty-five, came to the out-patient department of the Johns Hopkins Hospital on June 24, 1940. She was complaining of difficulty in defecation and a rectal discharge of three years' duration. In 1939, she had had a dilation of the rectal stricture at a hospital in Beckley, West Virginia. Following the dilation she had relief for several months and then her condition became gradually worse. When seen in our rectal clinic the lumen of the rectum was practically obliterated by a dense stricture beginning one and a half inches above the anal margin. There was a small dimple in the center which barely admitted the tip of a Kelly clamp. The surface was rough but not ulcerated. The Frei test was strongly positive. The stricture was gradually dilated and by July 1940, admitted a No. 14 Hegar dilator. From that date on she was used as a control and a Hegar dilator was inserted daily for a period of twenty minutes but no diathermy was used. She was given sixty-five treatments and left the clinic on October 11, 1940. At that time the stricture admitted a No. 18 dilator with ease and she was having no discharge. She returned to the clinic on May 5, 1941, seven months later. She had had no rectal discharge in the interim and had gained twenty pounds in weight.

Her bowels were moving daily and she had had no bleeding. The stricture had contracted slightly and admitted a No. 16 Hegar dilator with ease. The surface was smooth and there were no signs of ulceration.

It can be seen that all five of the patients treated showed local and symptomatic improvement at the conclusion of the course of diathermic dilatations. In one a rectovaginal fistula healed and has not recurred, in another, however, a rectovaginal fistula persisted unchanged.

Three to six months after treatment ceased the strictures had recontracted to some extent in all five of the patients treated. X-rays at this time showed little change from the original ones obtained before the instigation of treatment.

Two patients were used as controls and one of these (Case VII) showed the most marked improvement of any, and demonstrated little evidence of recontraction of her stricture. The other control showed temporary improvement at the end of her treatment but within three and one-half months the stricture had recurred to the same caliber as before therapy was begun.

#### CONCLUSIONS

From these facts we conclude that diathermy treatment *per se* to rectal strictures of lymphogranulomatous etiology, in our experience, offers very little if any curative effects. We believe that what benefits did result are primarily the effect of more frequent and prolonged dilatations that we had used in the past.



# URINARY CALCULI AND RECUMBENCY\*

ROBERT LICH, JR., M.D.

Chief of Genitourinary Surgery,  
U. S. Marine Hospital

AND

ROBERT MANSFIELD, M.D.

Chief of Surgical Staff,  
U. S. Marine Hospital

LOUISVILLE, KENTUCKY

THE close relationship between urinary calculi and recumbency is generally not adequately appreciated. Orthopedic surgeons often witness calculus in patients confined to bed for long periods. Medical men, too, find such cases now and again but are not generally cognizant of their frequency nor the methods of prevention. Hence, recumbency and calculi of the urinary tract are not commonly associated in the mind of the attending physician.

In a review of the various standard systems of medicine, surgery and pediatrics no mention of prophylactic care in reference to urinary stones was found in the sections on treatment of the different chronic disorders. However, the urological and surgical literature, both of this country and abroad, contains a number of articles on recumbency associated with urinary lithiasis. Wesson, in 1931, reported a series of cases in which twenty-three out of 150 men suffering with fracture of the femur developed renal calculi. Wallenstein reported a case of bilateral renal calculi five weeks after immobilization for a fracture of the spine. Mawson frequently found the condition in orthopedic patients eighteen months to fourteen years of age who were being treated for such disorders as tuberculosis of the spine and hip, slipped epiphysis, septic arthritis of the hip and knee, acute myelitis, spina bifida and celiac disease. Keyes, in 1936, found a 15 per cent incidence of urinary stones in 200 children examined in an orthopedic hospital. Goldstein and Abeshouse reviewed the literature and added fourteen additional cases. McCague made the observation in his series of ten cases that the average period in bed was five months, but that the diagnosis of stone

was not made until twenty months following the injury. To this list of contributors may be added the names of Crowell, de Faria, Pulvertaft, Armstrong, Webster, Wood, and Carlson and Ockerblad. From this brief review of the literature it is obvious that this condition, though not common, is far from being a medical curiosity.

In this paper four cases are recorded: First, a case of anterior poliomyelitis with several calculi in the renal pelvis which developed within three months while the patient was confined in a respirator; second, a patient developing a stone in a lower renal calyx that was diagnosed ten months following his injury, compound fracture of the tibia and fibula. Following a five-week convalescent period the patient complained of back pain intermittently but refused a urologic work-up until he was stricken with an acute stone colic. A third patient developed a silent hematuria following a fracture of both bones of the leg. Intravenous pyelography definitely established the diagnosis of multiple renal calculi. The fourth case was that of a chronically ill patient who developed a ureteral calculus after four years of interrupted invalidism. Previous pyelographic studies demonstrated conclusively that this stone developed during the patient's long illness.

## PATHOGENESIS

The etiology of renal calculi is a complex and controversial subject; however, in this particular phase of the subject there are observations which will aid us in our appreciation of the cause of renal calculi occurring in the bedfast patient. As is well known, when any bone in the body is not

\* From the Departments of Surgery and Urology, U. S. Marine Hospital, Louisville, Kentucky.

used, it undergoes a loss of some of its calcium salts, and when the muscular system is put at rest there occurs muscular atrophy with a concomitant reduction in the blood supply. Therefore, the reduced muscular blood supply creates a relative hyperemia of the bone, which in turn promotes rarefaction. Grieg has summarized this process as follows: "Maintain the circulation within certain limits and bone remains unchanged; produce a definite hyperaemia and bone undergoes rarefaction, decalcification, osteoporosis; restrict the blood supply and bone undergoes consolidation, increased density, osteosclerosis; cut off the blood supply and the bone undergoes necrosis."

Injury and infection produce local skeletal decalcification. Imperfectly mobilized fractures with constant trauma induced to the bone ends result in eventual rarefaction. Infection destroys bone as is seen, for instance, in finger felon or osteomyelitis.

Although calcium is not excreted primarily through the kidney, the urinary calcium is markedly increased during a period of bone decalcification. In the event that the urine becomes highly concentrated, the calcium salt may reach a point of supersaturation and initiate a precipitate of inorganic calcium. A so-called "mud-stone" is thus formed in the renal pelvis, ureter or bladder. If conditions are favorable, additional calcium is precipitated and the calculus grows until the entire renal pelvis may be filled, finally impairing kidney function.

This mechanism of salt precipitation from a saturated solution is effective in the production of calculi during recumbency, since most of these stones are composed of calcium phosphate. The carbonates, urates, and occasionally, oxalates, play a minor part in the composition of these calculi. When the calculus is complicated by infection a triple phosphate (ammonium magnesium phosphate) stone mixed with fibrin and other organic constituents occurs.

The rôle of infection in the precipitation of urinary salts is not a factor in this partic-

ular circumstance, since a large proportion of renal stones accompanying recumbency are found in sterile urine. When urinary infection is present it is usually introduced in one of four ways: (1) Urethral instrumentation; (2) ascending urinary infection due to uncleanliness, especially in the female; (3) infection of bone or other foci, delivered to the kidney via the blood or lymph; and (4) through constipation due to atonia of the abdominal musculature accompanying the inactivity of recumbency.

The exact rôle of vitamins in the etiology of calculi is a matter of conjecture. The fact that such authors as Osborne, Mendel, and Ferry, Grossman, Higgins, Livermore, Bliss, and Prather have reported that experimental animals develop renal calculi on vitamin A free diets is certainly no indication that vitamin A is essential in the prevention of urinary calculi. This latter point is particularly emphasized by Clausen, who suggests that the answer lies in a closer scrutiny of clinical records rather than animal experimentation.

The advocates of vitamin A deficiency believe that stones are formed in one of two ways: (1) the deficiency causes a metaplastic keratinization and desquamation of the urinary tract epithelium, thus supplying a nidus for crystalloid deposition (McCarrison; Higgins; Hryntshak; Steiner, Zuger, and Kramer); (2) the calculi form because dietary deficiency causes an alkaline urine with the resulting precipitation of salts (Higgins; Osborne, Mendel, and Ferry; Ravich).

Higgins has reported that in the Cleveland Clinic 68 to 74 per cent of the cases of renal lithiasis gave photometric evidence of vitamin A deficiency. Also, Ezickson and Feldman, in 1937, found that twenty-four out of their twenty-five cases of urinary lithiasis showed vitamin A deficiency. These results are interesting and suggest a possible association, but they do not constitute unquestionable proof. In fact, the work of Youmans, Jeans, and Zentmire shows that vitamin A deficiency goes hand-in-hand with an inadequate diet rather

than with any definite tendency to stone formation. In short, the problem of lithiasis and vitamin A deficiency is still unsolved.

#### SYMPTOMATOLOGY

Hematuria is the foremost symptom (macroscopic or microscopic finding) in urinary calculi associated with recumbency. Hematuria is usually first manifest when the patient's position is radically changed, that is, when the patient, after being bedfast for several weeks, is changed from the dorsum to the ventrum, or when he is allowed out of bed. Renal colic, another manifestation of urinary stone, is usually accompanied by a microscopic hematuria. However, in renal stone associated with enforced recumbency, kidney colic is far less common than is hematuria.

In some few cases renal calculi manifest their presence by the sudden appearance of chills and fever of unknown origin. This, of course, is indicative of an associated infection and a microscopic examination of urine will make the diagnosis. It must be remembered, however, that a true pyonephrosis may be present in conjunction with renal stones and the urine will give no hint of renal infection.

#### SIGNS

The renal calculus without infection does not afford diagnosis by any physical diagnostic signs. However, when obstruction occurs the usual sign of renal pelvic distention is present—tenderness to deep pressure at the costovertebral angle of the affected side.

The abdomen, even during acute attacks of renal colic, may or may not reveal evidence of muscle spasticity, though the patient often complains of a generalized abdominal tenderness to deep palpation.

#### DIAGNOSIS

The roentgen ray affords the only means of positive diagnosis. When the stone is suspected, and the usual flat plate of the abdomen reveals a suspicious shadow in

the path of the urinary tract, the diagnosis can usually be established by intravenous pyelography. Cystoscopy is contraindicated in the uninfected case because of the danger of introducing infection. For this reason, cystoscopy for diagnosis of renal stone formed during recumbency is definitely undesirable until the patient has been given ample opportunity to combat the condition by medical treatment in the form of urinary acidification for calculus dissolution.

#### TREATMENT

*Prophylaxis.* The prevention of renal stones is, of course, the prime consideration. In the recumbent patient it has been demonstrated repeatedly that uninfected renal calculi can be dissolved by urinary acidity (Pyrah and Fowweather). Hence it follows that, in the absence of infection, stones can be prevented. However, the factors of stone formation must be considered carefully in any form of therapy directed toward calculus prevention.

Decalcification of bone must be kept at a minimum. Decalcification can be best reduced by active movement of the parts of the body not involved by the primary disease process, and massage of the affected parts affords protection from local bone hyperemia and its consequent decalcification (Pyrah and Fowweather).

The fluid balance of the individual must be carefully controlled so that urinary salt precipitation is prevented. The patient must take at least 2,500 cc. of liquid daily, and more if the fluid loss is great due to such factors as fever, diarrhea, or vomiting. Heliotherapy must be controlled in order to avoid an excessive fluid loss. Boyd emphasizes particularly this factor of physiologic renal lavage.

The dietary regimen must be carefully planned through the entire course of the recumbent period. Since the diet must produce an acid ash, proteins are of very definite importance. Meats, fish and cereals should be included in the diet daily and vegetables and fruits should be intelli-

gently employed since they produce an alkaline urine.

The fluid administered must yield an acid ash, for it would be sheer folly to advise an acid ash diet and permit alkaline ash fluids to be taken freely. Fruit juices yield an alkaline ash, whereas barley water produces an acid ash. Fluids, then, such as barley water and those of neutral reaction such as water are to be preferred for the maintenance of urinary acidity. Urinary acidity is qualitatively, not quantitatively, important in calculus prophylaxis.

Repeated urinalyses are an essential part of the medical regimen. At weekly intervals urinary hydrogen ion content should be determined and certainly at intervals no longer than a month microscopic examinations of the urine should be done so that a stone will be discovered long before its subjective manifestations.

The value of vitamin A therapy in urinary calculi is still a moot question. However, since it seems that patients with stones often exhibit a vitamin A deficiency it may be advisable to estimate their vitamin saturation. To date there is no accurate method for estimating the amount of vitamin A, but the biophotometer serves to give at least a relative index (Cantarrow). Normally at least 3,000 International Units of vitamin A should be ingested daily by adults and at least twice that quantity by children. If this cannot be accomplished by the diet, vitamin A may be given as capsules of carotene in oil (Higgins). The intake of the other vitamins should be adequate in any satisfactory diet. Vitamin D should be administered as cod liver oil, since hypervitaminosis may play a rôle in calculus production (Putscher, Thatcher).

At not longer than forty-eight to seventy-two-hour intervals the patient must be made to change position completely. This constitutes moving the patient from the dorsum to the ventrum; the half way mark affords little, if any, benefit. Armstrong reports that in the two and a half years since he has made a practice of moving his patients at regular intervals, no urinary

tract complications have arisen. Furthermore, Pulvertaft claims that 27 per cent of urinary stones formed during recumbency disappear spontaneously if renal drainage is aided through the frequent change in position of the patient.

The unintelligent use of the urethral catheter is positively contraindicated in patients whose long recumbency is anticipated. Every means to initiate spontaneous urination in the individual who experiences acute urinary retention must be employed before resorting to catheterization with its almost certain aftermath of urinary infection. Methods employed to stimulate spontaneous urination are hot compresses to the suprapubic region, immersing the hand in warm water, letting the patient hear the flow of water, etc. If these methods should prove fruitless, one of the cholinergic drugs such as mecholyl, or even the more powerful doryl, may be employed. A fair trial of these methods should precede urethral catheterization. However, if the use of the catheter is imperative, it is important to give the patient immediately and for the following few days some suitable urinary antiseptic. Intravenous uritone is useful in the event of nausea or vomiting. The acid urinary antiseptics (methenamine with ammonium chloride or mandelic acid) are more desirable since urinary acidity should be maintained.

A properly selected diet will automatically produce an acid urine of sufficient intensity to keep urinary salts well in solution, but the unco-operative patient needs supplementary acid medication. Ammonium chloride, if tolerated, is a very effective urinary acidifier. In the event ammonium chloride is not well tolerated, acid ammonium phosphate or acid sodium phosphate may be prescribed in similar doses (Mitchel). Boyd, on the other hand, warns against the use of this drug because of its ability to create a phosphaturia.

Patients who require long periods of bed rest need careful supervision of the intestinal tract. Atony of the abdominal musculature favors constipation, which, in turn, is

often the forerunner of an *Escherichia coli* urinary tract infection. Also, such compounds as sodium bicarbonate and magnesium oxide must be judiciously prescribed, and this is true of saline cathartics containing phosphates and sodium bicarbonate (Boyd).

Calculus prophylaxis during enforced recumbency may be summarized as involving essentially three considerations: (1) adequate renal drainage and lavage; (2) the production of a urinary hydrogen ion content conducive to crystalline solvency, and (3) the prevention or early eradication of urinary tract infection.

*Stones in an Uninfected Urine.* The various factors discussed under prophylaxis should be carefully considered and followed in attempting to dissolve calculi in uninfected urine. The point of prime importance is the production and maintenance of a highly acid urine. A large fluid intake is essential and must be maintained even if parenteral fluids must be administered, the attempt being to dissolve the calculi by acidification and physiologic renal lavage. That this is possible has been demonstrated by Pyrah and Fowweather, Wesson, Pulvertaft, and by one of the authors (R. L.).

*Stones in Infected Urine.* Regardless of the amount of infection, this condition resolves itself eventually into a surgical problem. The fibrin and other organic material deposited in the stone matrix produce a body insoluble to any marked degree in any of the present day medications.

#### SUMMARY

1. There is a definite relationship between recumbency and urinary stones.

2. Factors for the prevention of renal calculi during recumbency are urinary acidity, urinary dilution, prevention of urinary stasis, and prevention of bone decalcification.

3. Aseptic urinary stones can be dissolved by urinary acidity and the maintenance of a sufficient urinary flow.

4. Renal stones in the presence of infection constitute a surgical problem.

5. Four cases of urinary calculi following recumbency, seen by the authors, are briefly mentioned.

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# PRIMARY MALIGNANT TUMORS OF THE TESTICLE\*

PHILIP ROSENBLATT, M.D.,

Resident in Pathology, Jewish Hospital of Brooklyn

DAVID M. GRAYZEL, M.D.

Associate Director of Laboratories, Jewish Hospital  
of Brooklyn

AND

MAX LEDERER, M.D.

Director of Laboratories, Jewish Hospital of Brooklyn

BROOKLYN, NEW YORK

WITHIN recent years the subject of intrinsic testicular neoplasms has attracted the renewed attention of investigators. Attempts at clarifying the confusion in classification have generally succeeded only in adding new terms to an already overburdened terminology.

The first description of a testicular tumor was that of St. Donat,<sup>1</sup> in 1696, who reported an obvious teratoma. No real progress was made until 1845 when Sir Astley Cooper<sup>2</sup> distinguished cystic from solid neoplasms and assigned the former a somewhat more favorable prognosis. Johnson,<sup>3</sup> in 1856, recognized the tridermal nature of some testicular tumors, but it remained for Langhans,<sup>4</sup> in 1887, to classify the tumors, with the aid of histological sections, according to their structure. He suspected that a large proportion of all testicular tumors were teratomatous, a view which Wilms<sup>5</sup> consolidated in 1896. Wilms further suggested that the homogeneous neoplasms represented an overgrowth of one germ layer which destroyed and obscured the remains of the other germ layers. This view was generally accepted until 1906 when Chevassu<sup>6</sup> sharply dissented. He divided testicular neoplasms into roughly equal halves, of which the one group comprised the teratomas. The second, consisting of homologous tumors, were considered to be anaplastic neoplasms originating in the germinal epithelium. This nonteromatous group he called "seminomes" to describe their origin.

The dualistic concept of Chevassu re-

mained unchallenged for only a short time. In 1911, Ewing<sup>7</sup> reviewed the subject and reverted to the unitarian concept of Wilms. He reaffirmed the teratomatous origin of practically all testicular tumors and stated that these tumors arose from misplaced primordial totipotent germ cells in the region of the rete testis. The seminoma of Chevassu he considered to be merely a one-sided overgrowth of a single germ layer and he termed it "embryonal cell carcinoma." Ewing described a case of embryonal carcinoma in which he found minute traces of cartilage which "would have been overgrown and eradicated by the rapidly advancing carcinoma."

Thalheimer and Geist,<sup>8</sup> and Eisendrath and Schultz,<sup>9</sup> however, continued to support Chevassu's dualistic concept and Bell<sup>10</sup> even described transition stages. Bell also added the term, spermatocytoma.

Robert Meyer<sup>11</sup> noticed the similarity of Chevassu's "seminoma" and Ewing's "embryonal carcinoma" to ovarian dysgerminoma. Meyer suggested the term "dysgerminoma of the testis" for this group since he believed that these tumors arose from undifferentiated germ cells that are found in the gonads before sex differentiation occurs. Thus he added another term to the already confusing terminology.

Many tumors of the testicle are associated with the presence of gonadotropic hormone in the urine. Biological assays were recommended by Ferguson,<sup>12</sup> in 1934, in order to clarify the study of testicular neoplasms. He states that the quantitative

\* From the Department of Laboratories, The Jewish Hospital of Brooklyn, New York.

determination of prolan A is a definite indication of the structural type of the tumor and that the more embryonal its

tumors, arising from neutral cells, therefore, are without hormonic influence. Thus, Christopoulos also uses hormone assays

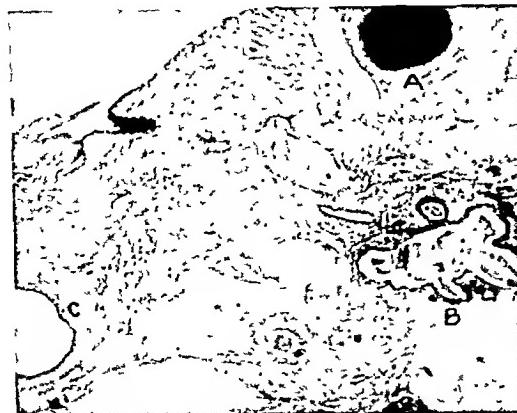


FIG. 1. Case XIII. Benign teratoma showing (A) cartilage, (B) structure resembling bronchiole, and (C) cysts lined with flat epithelium.  $\times 48$ .

character, the greater the output of hormone, and that the excretion of prolan A is increased by the presence of metastases.

In 1940, Melicow<sup>13</sup> presented a classification of testicular tumors on the basis of pathological embryology. He recognized teratological and nonteratological groupings, placing in the former, Ewing's embryonal carcinoma. In the latter group, under the new heading "malignant seminocarcinoma," he designated as a homonym, Chevassu's "seminoma."

Christopoulos<sup>14</sup> devised a classification in which he recognized the anatomical similarity between "seminoma" (dysgerminoma) on the one hand and "embryonal carcinoma" on the other. He believes that the latter are a monodermal development arising from cells of the somatic blastomere which had become included in the mesenchymal core of the testis during segmentation of the fertilized ovum and involution of the somatic blastomere. Tumors of this origin, he states, usually have hormonic influences. On the other hand, the group of dysgerminomas he considers not to be teratomas in the pure sense, since, like Meyer, he believes that they arise from neutral cells which are formed in the otherwise normally differentiated mesenchyme of the testis. These



FIG. 2. Case XVII. Chorionepithelioma metastatic to lung. Note large sheets of decidua-like cells.  $\times 300$ .

as one of the distinguishing criteria between Ewing's embryonal carcinoma and that anatomically similar group which is biologically inert and which he prefers to call dysgerminoma.

Gordon<sup>15</sup> recently reviewed a series of 142 cases and presented evidence favoring the teratomous origin of essentially all primary testicular neoplasms. He was unable to find any transitions between normal germinal epithelium and embryonal carcinoma (seminoma).

We were able to classify our twenty-nine cases as follows:

1. Heterologous tumors:
 

(a) Adult teratoma . . . . .	1
(b) Teratoma with malignant changes .....	6
(c) Chorionepithelioma..... . . . . .	2
2. Homologous tumors:
 

(a) Embryonal carcinoma .....	20
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Little difficulty was encountered in classifying the heterologous tumors. In the homologous group, however, no differentiation could be recognized anatomically between the embryonal carcinoma of the testis (Ewing) and the dysgerminoma (seminoma) of the testis (Meyer). Furthermore, no correlation could be established

between the histological picture and the biological properties of the tumors in this series. Ferguson<sup>12</sup> stated that in "em-

The teratoma with malignant changes is analogous to Ewing's embryoid or teratoid tumors. This group of neoplasms is made

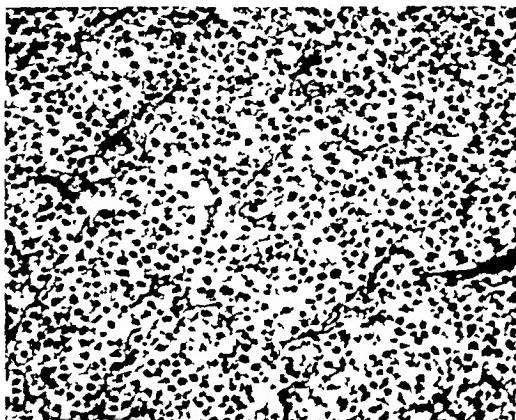


FIG. 3. Case xxix. Embryonal carcinoma without lymphoid stroma.  $\times 300$ .

bryonal carcinomas with lymphoid stroma" the excretion of prolan A in the urine is greater than in seminoma. A similar observation was made independently by Stevens.<sup>16</sup>

Aschheim-Zondek tests were done in eight cases in this series of homologous tumors; two were reported as positive and one as doubtful. In both cases with positive reactions the stroma was scanty and contained only scattered lymphocytes, whereas in some of those reported negative the lymphoid tissue and stroma were abundant.

Because of the difficulty experienced in differentiation either anatomically or by their biological behavior, it was decided to group them, as suggested by Ewing, under the all inclusive term of embryonal carcinoma of the testis.

**Pathology.** Teratoma is a complex tumor composed of tissues and organs derived from the three germ layers. An adult teratoma is one in which the tissues are fully differentiated and arrange themselves in an orderly fashion. These are relatively benign neoplasms and, according to Higgins and Buchert,<sup>17</sup> they constitute only 5 to 10 per cent of all teratomas. In our series, we found one adult teratoma in a group of nine heterologous tumors, an incidence of 11 per cent.



FIG. 4. Case xxvi. Embryonal carcinoma. Note accumulation of small round cells in follicle-like arrangement.  $\times 300$ .

up of tissues derived from two or more germ layers in which one or more elements show definite malignant tendencies. We usually append the descriptive term, "carcinomatous" or "sarcomatous" change, as the case may be. However, we do not place too great stress upon this feature because, due to its heterologous potentialities, the primary tumor or its metastases may in different places show combined carcinomatous, adenocarcinomatous or sarcomatous features. For example, one of our cases may be briefly reviewed:

**CASE V.** The patient was a twenty-seven year old married man, admitted September 11, 1938. He stated that in April, 1938, while pushing a hand truck, he felt a sharp pain in the right groin which extended to the testicle. One month later he noticed swelling of the right testis. During the four months prior to hospitalization, he had considerable pain in the

right groin and testis, and he noticed a variation in the amount of testicular swelling. On examination, an irregular tender mass was palpated in the region of the right epididymis. The testis was felt posterior and adherent to the mass.

The clinical impression was hematocele with tumor of the testicle to be excluded. Right orchidectomy was performed on September 12, and a hard nodular tumor mass was found extending into the testicle and involving almost the entire upper pole.

The testicle measured 7 by 4 by 3.5 cm. One area, 4 by 3 cm. was firm, and on section, pale grey in some places, dark brown and bright red in others. The remainder of the testicle was pink and soft. Here, the seminiferous tubules teased easily.

Microscopically, one portion showed tumor tissue and uninvolved portions of the testis. The former presented a variegated picture. In some areas there were nests of large polyhedral cells with abundant granular cytoplasm and large vesicular nuclei with one or more nucleoli. The cytoplasmic borders were distinct in some cells, indistinct in others. Mitotic figures were occasionally seen. In places, the cells were arranged in cords or nests, and even tended toward acinar formations. Tumor cells were seen within endothelial lined spaces. The stroma was broad and infiltrated with eosinophiles, small and large mononuclear cells, and some polymorphonuclear leukocytes. Other zones showed large spindle-shaped cells varying greatly in size and shape with large oval hyperchromatic nuclei lying in a loose, scant stroma densely infiltrated with cells as above. Still other zones showed both types of cells participating in the tumor formation. With the Van Gieson, Mallory's aniline blue, and Laidlow's connective tissue stains, the tumor tissue was seen to be made up of epithelial, connective tissue, and muscle cells. Diagnosis: Teratoma testis with carcinomatous and sarcomatous changes.

The Aschheim-Zondek test was repeated and was negative. The patient made an uneventful recovery and was discharged September 18. In May, 1939, he was again hospitalized because of pain in the right lumbar region of one week's duration. X-ray examination revealed right hydronephrosis. Right nephrectomy was performed. At this time it was noted that the middle third of the right ureter passed through

retroperitoneal nodular tumor tissue. The patient recovered from the operative procedure and was discharged June 11, 1939. The Aschheim-Zondek test was again reported as being negative. In September, 1939, the patient died at home with extensive metastases. The entire duration of the disease was about one year.

The chorionepithelioma is a curious tumor which is similar to the like tumor in the female. It is composed of syncytial masses of chorionic epithelium and unquestionably is the most malignant tumor of the testis. The primary growth is often very small and clinically unrecognized. Widespread hematogenous metastases, especially to the lungs, occur early and sudden hemoptysis may be the presenting symptom. The extremely high titer of gonadotrophic hormone in the urine of patients with chorionepithelioma is of great diagnostic and prognostic significance. Both patients died within seven months of the onset of symptoms despite vigorous therapy.

Ormond and Prince<sup>18</sup> state that in most series, heterologous and homologous tumors appear in almost equal numbers. In our series, however, only nine of twenty-nine neoplasms were heterologous, an incidence of 31 per cent.

In the homologous group of tumors we found no instances of pure sarcoma, such as have been described in the literature. We reviewed our old cases which were so diagnosed and were able to place them all into the group of embryonal carcinomas.

The homologous tumors are composed of large round to polygonal cells with scanty cytoplasm and poorly defined cell membranes. The nuclei are large, round to oval in shape, and vesicular in character. As a rule, the constituent cells are loosely arranged in irregular alveoli demarcated by a fibrillar stroma. Lymphocytic infiltration may be marked, but is often absent. Areas of hemorrhage and necrosis are common and occasional giant cells are seen.

In our series, the embryonal carcinoma comprised 69 per cent of the entire group.

*Incidence.* Malignant tumors of the testicle are rare. At the Henry Ford Hospital, Ormond and Prince<sup>18</sup> report that of

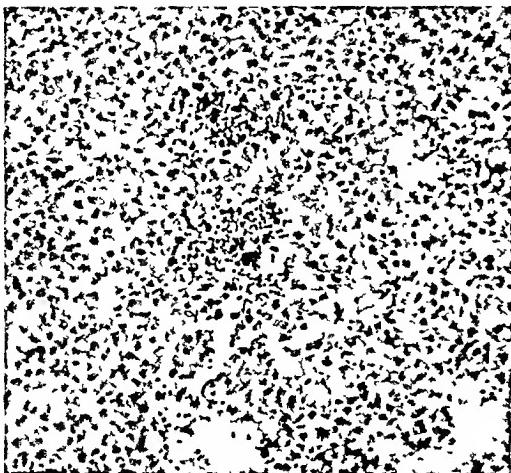


FIG. 5. Case 1. Embryonal carcinoma with diffuse scatterings of small round cells.  $\times 300$ .

319,000 men, women and children treated since its founding in 1915 only twenty-one malignant testicular tumors were found. MacKenzie<sup>19</sup> reports twenty-seven cases in 307,174 admissions at the Royal Victoria Hospital. At the Jewish Hospital of Brooklyn, since 1915, we have found twenty-nine cases in 169,600 general hospital admissions excluding children, obstetrical cases and newborns.

*Age.* Malignant tumors of the testicle appear most frequently during the period of greatest sexual activity, that is between the ages of twenty and fifty years. In the series reported by Higgins and Buchert,<sup>17</sup> 87.5 per cent of the cases occurred in this age group. Dean<sup>20</sup> reported a series of 292 cases in which the patients varied in age between one year and seventy, the average being 33.5 years. Forty-three per cent of the patients were between twenty-five and thirty-five years of age at the time of the first symptoms while 80 per cent were less than forty. In our series, the youngest patient was fifteen while the oldest was seventy-two years of age. In the series reported by Gilbert and Moody,<sup>21</sup> the average age at the time of onset was thirty-one years, and 86 per cent occurred between the ages of twenty and fifty years. In our

series, 86.2 per cent of our cases fell between the age limits of twenty and fifty years.

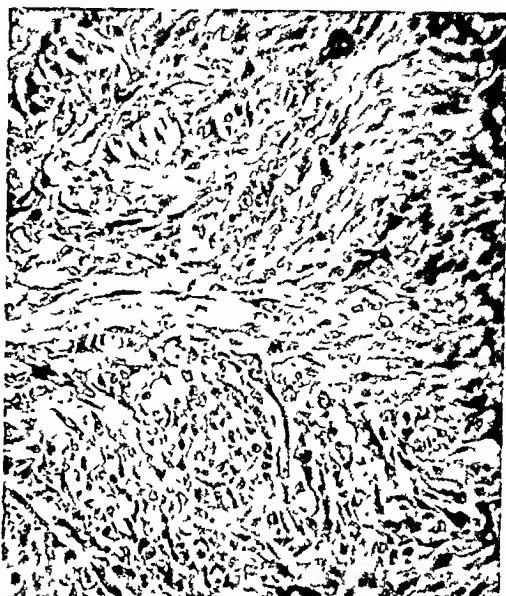


FIG. 6. Case v. Teratoma with sarcomatous change.  $\times 300$ .

Simpson<sup>22</sup> reports the greatest incidence of teratoma between twenty and thirty years, while that of seminoma is between thirty and forty years. In our series, the average age incidence in the group of heterologous tumors was twenty-seven years, while that of the homologous neoplasms was 37.2 years. This would seem to indicate that the teratomas appear in an earlier age group than the embryonal carcinomas.

*Side Involved.* Reports in the literature vary as to the predominance of tumors in the right or left testicle, but all agree that bilateral involvement is rare. In Dean's<sup>20</sup> series, the right side was involved in 52.2 per cent of cases, the left in 47.6 per cent. He stated that the difference could be accounted for by the greater frequency of undescended testicle on that side. In the series of Gilbert and Moody, the right side was involved more frequently than the left. In addition, he reported two cases of bilateral growths. We found the right side involved sixteen times (55 per cent), the left thirteen times (45 per cent).<sup>23</sup>

**Trauma.** The relation of trauma to tumor in the testis is also of great interest from a medicolegal point of view. Injury to the testicles is common and it is easy to attribute enlargement of the organ to a preceding trauma. Most authorities, however, seem to believe that physical insult to the testicle, while it may call attention to a growth hitherto unnoticed or excite more rapid growth in a small pre-existing tumor, can hardly arouse malignant degeneration in a previously normal organ.

The incidence of trauma in different series varies rather widely: Kirshbaum and Jacobs,<sup>23</sup> in thirty cases, report an incidence of 36.8 per cent; Higgins and Buchert<sup>17</sup> report 19.2 per cent; in Dean's<sup>20</sup> series of 124 cases the incidence of trauma was 11 per cent, while Rea<sup>24</sup> reviewing seventy-six cases, observed that 38 per cent of his patients had experienced definite trauma. In our series only three patients gave a history of previous injury to the testicle, an incidence of 10.3 per cent.

**Duration of Symptoms.** The testicle is a very prominent organ and it would commonly be supposed that recognition of disease would be early. Surprisingly enough, this is not the case and many patients procrastinate for an extremely long time before seeking medical advice. In most series, the average elapsed time between the onset of symptoms and medical consultation is one year to eighteen months. In our series, advice was sought from two weeks to fifteen years after the onset of symptoms, the average being 15.2 months.

**Clinical History.** It is said that there are no pathognomonic signs or symptoms of a malignant tumor of the testicle. The first symptom ordinarily noted is an increase in size of the testicle, this being painless and accompanied by a feeling of weight or fullness in the scrotum. In 92 per cent of the 124 cases reported by Dean,<sup>25</sup> in 83 per cent of the cases reported by Higgins and Buchert,<sup>17</sup> increase in size of the testicle was the first sign. In our series, fifteen patients (53.6 per cent) presented themselves because of painless enlargement of

the testicle. In Tanner's<sup>26</sup> series, 52 per cent of the patients complained of pain, while twelve (41.4 per cent) of our patients suffered from this symptom.



FIG. 7. Case v. Teratoma with carcinomatous change.  $\times 300$ .

Constitutional symptoms such as weakness, pain in the back, anorexia and loss of weight are almost invariably manifestations of metastases. In Case IV the patient complained of back pain in addition to testicular symptoms. In this instance the patient died with widespread retroperitoneal metastases. Case VII initially complained of coughing up a large blood clot and x-ray examination revealed metastatic nodules in the lungs. Attention to the testicular neoplasm in Case XXIV was attracted by symptoms of prostatism. The testicle was found to contain a hard nodular mass and was removed in the course of the first-stage prostatectomy. The real nature of the testicular mass became apparent only after histological examination.

**Follow-up of Cases.** Higgins and Buchert<sup>17</sup> state that a review of the literature and of their own cases leads them to the conclusion that the end results of treatment in cases of malignant tumors of the testicle are quite discouraging. In the series of Gilbert and Moody,<sup>21</sup> only three of twenty-one patients were alive with an average survival period of thirty-one months. Ormond and Prince<sup>18</sup> found the prognosis best in those patients who had no visible

## TABULATION OF DATA ON TWENTY-NINE CASES OF TESTICULAR NEOPLASM

CASE NO.	AGE	PRES-SENTING SYMPTOM	DURATION	SIDE	TRAU-MA	ASCH-HEIM-ZON-DEK TEST	ORCHI-DEC-TOMY	X-RAY THER-APY (PRE-OP. POST-OP.)	MET-ASTASES ON ADMIS-SION	ORIGINAL PATHO-LOGICAL REPORT	FINAL PATHO-LOGICAL REPORT	FOLLOW-UP TO JULY, 1941
I	33	Swelling of testis	3 mos.	L	No	Positive	Yes	Post-operative	No	Embryonal carcinoma	Embryonal carcinoma	Died in 2 years
II	36	Swelling of testis	1 yr.	R	No	Negative	Yes	None	No	Embryonal carcinoma	Embryonal carcinoma	Well 3 years
III	21	Swelling of testis	2 wks.	R	No	....	Yes	Post-operative	No	Teratoma with malignant changes	Teratoma with malignant changes	Died in 2 years
IV	49	Swelling of testis; pain; back pain	7 wks.	L	No	Negative	Yes	Post-operative	Yes	Embryonal carcinoma	Embryonal carcinoma	Died in 10 mos.
V	27	Swelling of testis; pain	5 mos.	R	No	Negative	Yes	None	No	Teratoma with malignant changes	Teratoma with malignant changes	Died in 18 mos.
VI	32	Swelling of testis; pain	1 mo.	L	Yes	Positive	Yes	Pre-operative	No	Chorionepithelioma	Chorionepithelioma	Died in 8 mos.
VII	21	Hemoptysis; cramping abdominal pain; loss of weight	4 mos.	R	No	Positive	No	Yes	Yes	Chorionepithelioma	Chorionepithelioma	Died in 4 mos.
VIII	26	Swelling of testis; pain	9 mos.	R	No	Positive	Yes	Pre-operative	No	Embryonal carcinoma	Embryonal carcinoma	Well 5 yrs.
IX	37	Swelling of testis	1 yr.	R	No	....	Yes	Post-operative	No	Embryonal carcinoma	Embryonal carcinoma	Died in 1 year
X	36	Swelling of testis	6 mos.	L	No	....	Yes	Post-operative	No	Embryonal carcinoma	Embryonal carcinoma	Well 6 years
XI	33	Swelling of testis; pain	8 mos.	L	Yes	....	Yes	....	No	Embryonal carcinoma	Embryonal carcinoma	Well 7 years
XII	34	Swelling of testis	6 mos.	R	No	Negative	Yes	....	No	Teratoma with malignant changes	Teratoma with malignant changes	Well 7 years
XIII	26	Swelling of testis; pain	5 mos.	L	No	....	Yes	No	No	Spermatocytoma	Adult teratoma	Well 11 years
XIV	32	Swelling of testis; pain	4 mos.	L	No	....	Yes	Post-operative	Yes	Embryonal carcinoma	Embryonal carcinoma	?

## TABULATION OF DATA ON TWENTY-NINE CASES OF TESTICULAR NEOPLASM—(Continued)

Case No.	Age	Pre-senting Symptom	Duration	Side	Trauma-	Aschheim-Zon-deck Test	Orchi-dec-tomy	X-ray Ther-apy (Pre-op. Post-op.)	Me-tas-tases on Ad-mis-sion	Original Patho-logical Report	Final Patho-logical Report	Follow-up to July, 1941
xv	35	Swelling of testis; pain	5 mos.	L	No	....	Yes	....	No	Teratoma with ma-lignant changes	Teratoma with ma-lignant changes	?
xvi	29	Swelling of testis; pain	15 yrs.	R	No	Nega-tive	Yes	Pre-oper-ative	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Died in 1½ years
xvii	29	Swelling of testis	3 yrs.	R	No	....	Yes	Post-oper-ative	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Died in 22 years
xviii	43	Swelling of testis	3 yrs.	R	Yes	....	Yes	....	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Well 3 years
xix	21	Swelling of testis	3½ mos.	R	No	....	Yes	....	No	Teratoma with ma-lignant changes	Teratoma with ma-lignant changes	Died in 2 years
xx	26	Swelling of testis	6 mos.	R	No	....	Yes	Post-oper-ative	No	Teratoma with ma-lignant changes	Teratoma with ma-lignant changes	Died in 3 years
xxi	36	Swelling of testis	2 mos.	R	No	....	Yes	Post-oper-ative	Yes	Sarcoma	Embry-onal car-ci-noma	Died in 3 years
xxii	22	Swelling of testis	4 mos.	L	No	....	Yes	....	No	Sarcoma	Embry-onal car-ci-noma	?
xxiii	70	Swelling of testis; pain	11 wks.	L	No	....	Yes	....	Yes	Sarcoma	Embry-onal car-ci-noma	?
xxiv	72	Dysuria; dribbling	3 yrs.	L	No	....	Yes	....	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	?
xxv	15	Swelling of testis; pain	5 wks.	L	Yes	....	Yes	Post-oper-ative	No	Sarcoma	Embry-onal car-ci-noma	Died in 4 mos.
xxvi	34	Swelling of testis	1½ mos.	R	No	Nega-tive	Yes	Post-oper-ative	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Well 1 year
xxvii	27	Swelling of testis; pain	1 yr.	L	No	....	Yes	....	No	Sarcoma	Embry-onal car-ci-noma	?
xxviii	38	Swelling of testis	3 yrs.	R	No	Nega-tive	Yes	Post-oper-ative	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Recent
xxix	24	Swelling of testis	1½ mos.	R	No	Doubt-ful	Ycs	Post-oper-ative	No	Embry-onal car-ci-noma	Embry-onal car-ci-noma	Recent

metastases at the time of orchidectomy and who received radiation therapy post-operatively. Higgins and Buchert<sup>17</sup> also found a distinct margin in favor of those patients who received *x-ray* therapy plus orchidectomy.

Ferguson<sup>12</sup> cites Dean as reporting five-year cures in 29.2 per cent of a series of 154 patients treated with *x-ray* alone. Coley<sup>27</sup> reports favorable results by the combined use of orchidectomy and his streptococcus and bacillus prodigiosus toxin. Hinman<sup>28</sup> and Young<sup>29</sup> prefer the radical operation, despite its operative mortality rate of close to 5 per cent. In general, it can be stated that no matter what therapy is employed, the prognosis should be guarded.

In our own series, we were able to obtain follow-up data in twenty-three of twenty-nine cases. Of these thirteen patients died with a survival period ranging from four months to twenty-two years after the onset of the disease. Excluding the latter case, the average period of survival was seventeen months.

The case of the patient who survived twenty-two years is of such unusual interest that it is reported briefly below:

**CASE XVII.** No. 156584. The patient was first admitted to the hospital on February 9, 1911, at the age of twenty-nine years, with a three-year history of painless enlargement of the right testicle. Simple orchidectomy was performed and a diagnosis of round-cell sarcoma was made on the pathological specimen (re-check showed this to be an embryonal carcinoma).

In November, 1922, eleven years following the procedure, he was admitted to another hospital because of pain in the right upper quadrant of the abdomen. A diagnosis of retroperitoneal sarcoma was made and he was given a course of deep *x-ray* treatments.

He was seen again at this hospital twice in 1923 and in 1924, at which times indefinite masses were palpable in the right lower abdominal quadrant and in the hypogastrium. These masses were not tender and immobile. The patient was given another course of *x-ray* therapy between his third and fourth hospitalizations.

The patient was admitted to this hospital for the last time January 20, 1933, with a four-weeks history of increasing dyspnea, dependent edema, swelling of the abdomen, hemoptysis and severe abdominal pain. He expired March 29, 1933, and an autopsy was obtained. The postmortem findings included malignant thromboses of the left renal and spermatic veins, mesenteric and portal veins, and metastatic embryonal carcinoma in the liver and in the peripancreatic lymph-nodes.

Obviously, this patient developed metastases eleven years following orchidectomy, which, however, were controlled by radiation therapy for another period of eleven years before he died of recurrences.

Of the thirteen patients who died, seven were in the group of homologous tumors, while six were heterologous. Of the ten patients who are alive at this time, two may be excluded because they are too recent to be significant. Amongst the remaining eight cases, six were homologous neoplasms, and two heterologous. One of these heterologous tumors was the instance of adult teratoma, and this patient is alive and well eleven years following orchidectomy.

In analyzing these figures, one is immediately impressed with the high mortality in the group of heterologous neoplasms. Despite vigorous postoperative *x-ray* therapy and the absence of metastases on admission, all died within three years of the onset of symptoms. The two patients with chorionepithelioma expired four months and eight months after the onset of the disease, respectively.

In the survival group of ten cases, two instances of embryonal carcinoma are excluded from analysis because of their recent vintage. Of the remaining eight cases, as noted above, two were in the heterologous group but only one showed malignant changes. This patient is alive and well seven years following orchidectomy, despite the fact that no radiation therapy was given. The average life span following orchidectomy in these eight instances is five and one-third years.

## CONCLUSIONS

1. Testicular tumors occur most frequently between the ages of twenty and fifty years.
2. Heterologous tumors appear in an earlier age group than the homologous neoplasms.
3. Bilateral testicular neoplasms are rare. The right testicle is more frequently involved than the left.
4. In our series trauma was reported in 10.3 per cent of cases.
5. The average duration of symptoms in our series was 15.2 months before medical advice was sought.
6. There are no pathognomonic signs of testicular neoplasm, but painless enlargement is the most common presenting symptom.
7. The heterologous tumors offer a poorer prognosis than the homologous neoplasms.

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# VITAMIN K AND ITS RÔLE IN BLOOD COAGULATION\*

ARTHUR J. D'ALESSANDRO, M.D.

Assistant and Lecturer in Postgraduate Surgery, New York University Medical School

NEWARK, NEW JERSEY

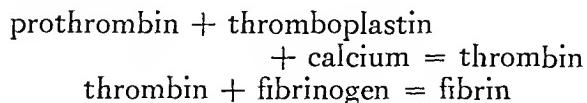
**T**HIS review will present our present concept of the mechanism of blood coagulation, a brief discussion of the factors involved in blood coagulation and a more detail discussion of the experimental and clinical uses of vitamin K.

## MECHANISM OF NORMAL BLOOD COAGULATION

Plasma contains a substance, *prothrombin*, which is activated in the presence of calcium and a platelet or tissue factor, *thrombokinase*, to form an active coagulant, *thrombin*. Thrombin reacts with *fibrinogen* to form an insoluble split product *fibrin* in the network of which the formed elements and serum are enmeshed to form an elastic structure, the blood clot. This is the classical Wöhlsch theory, based on the elementary facts of coagulation first established by Schmidt in 1893, and extended by the work of Hammersten and others.

Out of the multiplicity of divergent views of blood coagulation, there are two well established fundamental facts: (1) The formation of thrombin from its precursors (prothrombin, calcium and thrombokinase), and (2) the conversion of fibrinogen to fibrin under the influence of thrombin.

The facts can be expressed in the form of equations:



The relation of these reagents, calcium, thrombokinase, prothrombin, thrombin and fibrinogen along with other coagulants and anticoagulants to coagulation will be briefly summarized.

**Calcium.** A deficiency of calcium has not been found in hemorrhagic diseases.

Even in the marked hypocalcemia of parathyroid insufficiency no alteration of the blood clotting can be demonstrated. Similarly, the high blood calcium in hyperparathyroidism does not bring about any appreciable change in the coagulation time. Calcium in its ionized state was previously considered indispensable as one of the precursors of thrombin but more recent investigations have shown it to act in the organically combined state. Quick has recently brought forth evidence indicating that the important calcium factor is intimately tied up with the prothrombin molecule.

**Thrombokinase.** Thrombokinase is one of the most widely distributed elements involved in blood clotting occurring plentifully in almost all tissues and being highly concentrated in brain, lung tissue and blood platelets. It is absent in the circulating blood except in abnormal conditions when it immediately activates prothrombin to thrombin. It is thought to be a protein phospholipoid compound. As its name implies, its action in activating prothrombin is supposedly of an enzymatic nature. Eagle believes that the rôle of platelets in initiating coagulation in shed blood has been exaggerated and that the thromboplastic factor of greatest importance is a dissolved plasma constituent. This theory is supported by the recent work of Lenngenhager in 1936 which indicates that platelet disintegration may be the result, rather than the cause of coagulation. He believes that the thromboplastic material primarily responsible for coagulation is present in the plasma as a dissolved material, which is activated by contact with a foreign surface to form the actual thrombokinase. In support of this theory is cited the fact that

\*Read at the Surgical Seminar at New York University.

mammalian plasma carefully drawn and devoid of all cellular elements including platelets usually does clot. Patek and Stetson also found that normal cell-free plasma contains a factor associated with the globulin fraction. If this is added to hemophilic blood the blood is rendered normally coagulable. This factor may well be the thromboplastic substance of Lennghenager and this factor is now suspected of being deficient in hemophiliacs rather than any increased platelet stability as previously supposed.

*Prothrombin.* Prothrombin has been one of the least understood reagents in the chemistry of blood coagulation. Recent developments following the discovery of vitamin K have thrown considerable light on this substance. It is now known that it is essentially a product of liver metabolism, although it may be obtained from bone marrow as well and its concentration in the blood is directly dependent upon the assimilation of vitamin K. As the precursor of thrombin a deficiency of prothrombin results in a diminished blood coagulation.

The plasma concentration of prothrombin is indirectly determined by various tests such as that of Quick or Warner, Brinkhous and Smith.

*Thrombin.* Although not a normal constituent of blood plasma, thrombin may be found in minute quantities through the interaction of its precursors (prothrombin and thromboplastin). On this basis Howell has postulated the presence of an anticoagulant normally in the blood. The latest evidence indicates that prothrombin and thrombin are both carbohydrate containing proteins.

*Fibrinogen.* Fibrinogen is one of the best understood elements in coagulation. It is a protein known to be formed in the liver and normally present in the blood plasma in concentrations of 0.3 to 0.7 per cent. Fibrinogen is normally present far in excess of the amount necessary for coagulation. Only a few isolated reports of cases have appeared in which fatal hemorrhage could be attributed to a lack of fibrinogen

in the blood. Synthesis of fibrinogen is one of the last products of metabolism to be abandoned by a diseased liver. Bancroft and his co-workers noted that the fibrinogen concentration of human plasma is higher in infectious diseases and lower in profound liver disturbances. They believe that a fibrinogen concentration of over 0.8 per cent predisposes to phlebitis when associated with infection.

The exact mechanism of the thrombin-fibrinogen reaction has not yet been clarified. There is a growing belief in an enzyme action in transformation of prothrombin into thrombin in the presence of calcium as the first stage of blood coagulation; then thrombin in turn behaves as an enzyme in activating fibrinogen to fibrin. However, the recent work of Mertz, Seegers and Smith in demonstrating a linear relationship in the utilization of prothrombin and thrombokinase in the formation of thrombin casts some doubt on the enzymatic nature of this phase of coagulation.

*Anticoagulant.* One of the most complex problems in the mechanism of blood coagulation concerns the presence of a physiological anticoagulant. Many theories have postulated the presence of a physiological anticoagulant, which, until the discovery of heparin in 1916, defied all experimental verification.

*Coagulant.* In 1939, Seegers, Warner, Brinkhous and Smith obtained a remarkably effective solution of thrombin which is used as a hemostatic agent for the uncontrollable oozing which accompanies certain types of surgery, especially in patients with diminished blood coagulation. The solution, 1 cc. of a 1 per cent solution which will clot 1 cc. of blood in two seconds, is used as a spray on the operative field and is especially good in controlling bone bleeding and in cranial surgery. Bleeding from incised liver tissue was checked in five seconds or less. Clinical application of this agent is pending further investigation due to a difficulty in sterilizing the solution.

In concluding the discussion of the elements concerned in coagulation, until more

is known about the true nature of prothrombin and thrombin, our concepts of blood coagulation must remain in the realm of theory. Even theory has not as yet correlated all the experimentally confirmed facts.

#### HISTORY OF VITAMIN K

*Hemorrhagic Disease of Chicks.* In 1929, Henrik Dam, of Copenhagen, first reported a hemorrhagic disease in chicks reared on a fat-free diet. Similar observations were made by MacFarlane, Graham and Richardson in 1931 and Holst and Hallbrook in 1933. The blood of these chicks, when allowed to stand overnight, failed to clot. A vitamin C deficiency was suspected though lemon juice was not curative.

In 1934, Dam and Schönheyder reported that ascorbic acid, cod liver oil and wheat germ oil failed to influence the hemorrhagic tendency, thus eliminating vitamins C, A, D and E as etiologic factors.

In 1935, Dam named the etiologic factor of this hemorrhagic disease, the "koagulation vitamin" or vitamin K.

*Vitamin K and Prothrombin.* Since the addition of normal plasma to blood of bleeding chicks restored the coagulation time to normal, the defective element must reside in blood plasma. Dam, Schönheyder and Tage-Hansen succeeded in demonstrating that the defective element was prothrombin. Similar reports were simultaneously and independently published by Almquist and Stokstad, and Quick in this country.

*Prothrombin Tests.* The association of vitamin K with prothrombin was readily followed by the development of more accurate tests for prothrombin than were possible by the old Howell method. Most noteworthy of these new tests was that published by Quick in 1935 and the dilution test of Warner, Brinkhous and Smith reported a short time later. Both tests utilize the addition of excess tissue factor to recalcified blood plasma. The prothrombin levels are reported in percentage deviation from the eighteen to twenty-two seconds

required by normal plasma to coagulate. The bleeding tendency, however, may not become manifested until the prothrombin levels fall to below 30 or 20 per cent of normal.

*Vitamin K and Bacteria.* In 1936, Almquist and Stokstad of California and two years later Almquist, Pentler and Mecchi presented evidence that micro-organisms are capable of synthesizing the vitamin in food, feces or in pure culture.

*Jaundice and Prothrombin.* Although Wedelius, in 1683, first reported a death from bleeding in a jaundiced patient, the cause of cholemic bleeding remained unknown until 1937 when Quick postulated that the coagulation defect was due to a prothrombin deficiency. Experimental investigations immediately confirmed this fact with the result that cholemic bleeding, heretofore responsible for an average of 15 per cent of all deaths on biliary tract surgery, is now a rarity.

*Vitamin K and Bile Salts.* Hawkins and Brinkhous observed in the course of their experiments upon dogs with biliary fistulas in 1935 and 1936 that the bleeding tendency in these dogs was associated with low plasma prothrombin, which could be restored to normal merely by returning bile to the intestinal tract. Meanwhile Greaves and Schmidt were conducting experiments indicating the necessity of bile for adequate absorption of fat-soluble vitamins A, D and E, and now vitamin K was added to this group. The action of bile salts is purely a physical one. Early in 1938 clinical evidence began to accumulate indicating that fat-soluble vitamin K was required by all species and was not limited to birds and that the presence of bile in the intestine was essential for its absorption.

By 1938, Brinkhous, Smith and Warner in Iowa, Dam and Glavind in Copenhagen, and Snell, Butt and Osterberg of the Mayo Clinic, all had succeeded in restoring the prothrombin levels in jaundiced patients and in correcting the bleeding tendency by the administration of bile salts and vitamin K.

*Vitamin K and Liver.* Smith, Warner and Brinkhous next reported on the harmful effect of chloroform poisoning of the liver on the plasma prothrombin, which was seen to fall to as low as 5 per cent of normal after ninety minutes of chloroform anesthesia in a dog. Under these circumstances the blood fibrinogen is not affected. Similar drastic drops in plasma prothrombin was shown to follow partial or total hepatectomy in dogs, indicating that an adequately functioning liver is essential for the utilization of vitamin K in the production of prothrombin. Autopsy findings of extensive liver damage, from one cause or another, in those patients who failed to respond to the usual vitamin K therapy further confirmed this association of liver and prothrombin production.

*Vitamin K and Hemorrhagic Disease of the Newborn.* Rodda, in 1920, called attention to the defective coagulation of blood in infants in the first few days of life, but no explanation was offered until 1937 when Brinkhous, Smith and Warner reported that the blood prothrombin level of infants is very low when compared with adult values, the average being about one-fourth the adult concentration. It has been shown that the infant blood prothrombin falls from the second to fourth or sixth day of life when it may again reach the birth level, but does not reach the adult level until about the end of the first year. This fall is even more pronounced in premature infants. It is a well known fact now that vitamin K is produced by bacterial action. Logically it follows that as soon as the baby ingests food or water, it infects its intestinal canal, which at birth is sterile. With the establishment of an intestinal flora the synthesis of vitamin K begins, thus producing a rise in prothrombin after the first week of life. This explanation might account for Javert's observation that hemorrhagic disease is twice as common in babies born in the New York Hospital, where feedings were prepared according to the most sanitary methods, as in babies born at home.

In 1939, Waddell, Guerry, Bray and Kelley reported on the administration of vitamin K concentrates to two infants with very low prothrombin levels and prolonged coagulation time with the dramatic and rapid restoration of normal values. More extensive clinical evidence promises a marked reduction in the incidence of hemorrhagic disease in the newborn, now estimated at one in every 200 births. Hellman and Shettles found that the low prothrombin levels usually prevailing in newborn infants could be elevated by administering the vitamin to mothers prior to delivery.

*Synthesis of Vitamin K.* The developments in vitamin K in the past year have been chiefly concerned with the isolation, purification and synthesis of this important new vitamin. For most of this work the world is indebted to Doisy, McKee and their co-workers. Thus in five years we have witnessed developments, the ultimate appreciation and implications of which will not be realized for some years to come.

#### CHEMISTRY

*Natural Vitamin K.* The original vitamin K concentrates were obtained from alfalfa by Dam and from putrefied fish meal by Almquist. In 1939, Doisy and his associates isolated two distinct substances from these sources; naming the one from alfalfa vitamin K<sub>1</sub>, and that from fish meal, vitamin K<sub>2</sub>, as both had the same biologic activity in different degree. The common denominator of both vitamins was a 1, 4-naphthoquinone.

*Synthetic Vitamin K.* In 1939, Almquist and Klose reported on the use of synthetic phthiocol which is water soluble and could be administered intravenously without the need of bile salts. The natural phthiocol is a normal metabolic product of the tubercle bacillus. Soon many more vitamin K-active naphthoquinone derivatives were reported, of which 2-methyl-1, 4-naphthoquinone is the most potent and the one most commonly used clinically today. This product is also water soluble and much more potent

than natural vitamin  $\kappa$  or phthiocol. Synthetic vitamin  $\kappa$  is the first example in the discovery of vitamins in which the

mations, which, like potential shock, can be detected only by laboratory methods. One can readily realize how a nonbleeder

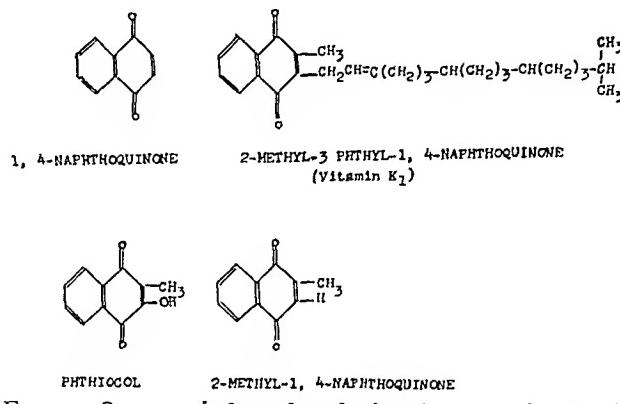


FIG. 1. Structural formula of vitamin  $K_1$  and related compounds.

synthetic substance is of greater biologic activity than the pure natural vitamin. (Fig. 1.)

#### PHYSIOLOGY

*Vitamin K and Prothrombin.* Just what happens to the vitamin after its absorption from the intestinal tract is not known. Vitamin  $\kappa$  is not a component part of the prothrombin molecule and the interaction of tissues, or more specifically liver, is necessary for the conversion of vitamin  $\kappa$  to prothrombin. The rapidity of action of vitamin  $\kappa$  as reflected by the response in prothrombin formation, suggests an enzymatic reaction. A deficiency of vitamin  $\kappa$  results in a corresponding fall in plasma prothrombin until a critical level is reached when spontaneous hemorrhages ensue.

*Prothrombin and Liver.* Animal experiments indicate that tissue injury in general is followed by a prompt and significant fall in the plasma prothrombin. The liver differs from other tissues in that it has been found to be essential for the formation of prothrombin. On the basis of this fact there is an explanation for the increased incidence of postoperative bleeding following difficult operations on the biliary tract despite the fact that there had been no previous bleeding tendency. It also emphasizes the necessity of determining potential bleeding by prothrombin esti-

with a plasma prothrombin of 30 or 40 per cent of normal, having a 25 per cent drop immediately after operation, might fall below the critical level and uncontrollable bleeding take place during the critical three to seven days postoperatively when there is a dietary deficiency as well.

As to the fate of prothrombin in the body aside from its rôle in the coagulation of the blood little is known. Andrus, Lord and Kaner have demonstrated that the blood in pulmonary veins has approximately 10 per cent less prothrombin than the blood in the pulmonary arteries, thus indicating that there is some destruction or loss of prothrombin in the pulmonary circulation.

The available evidence points to a continuous and relatively rapid disappearance of prothrombin from the circulation and concurrent formation of prothrombin which occurs mainly, if not exclusively, in the liver.

*Vitamin K Deficiency Syndromes.* Since a deficiency of vitamin  $\kappa$  is reflected in the plasma prothrombin, the deficiency syndromes may be theoretically determined from any condition likely to result in a hypoprothrombinemia. Such a condition may result from any of the following: (1) Lack of vitamin  $\kappa$  in the diet; (2) absence of bile salts from the intestinal tract; (3) grossly deficient absorptive surface of the intestinal tract; (4) marked liver

damage, and (5) marked and repeated hemorrhage.

#### CLINICAL USE OF VITAMIN K

Vitamin K may be used in any case presenting evidence of a hypoprothrombinemia with or without the hemorrhagic tendency if not due to extensive liver damage, in which case it is not contraindicated, but has been shown to yield little or no response. In the absence of obstructive jaundice, external biliary fistula or an abnormal intestinal surface, the prothrombin response to vitamin K may be interpreted as a test of liver function. Inability to correct a hypoprothrombinemia by vitamin K therapy is indicative of extensive liver damage.

Vitamin K is being used prophylactically in obstetrical practice. The prothrombin level of infants born of mothers treated with vitamin K has been found to be higher than in the nontreated group.

*Sources of Vitamin K.* The average human diet contains adequate amounts of vitamin K for normal requirements if it can be absorbed and utilized. Rich sources of natural vitamin K are spinach, kale, cabbage, egg yolk, rice bran, tomatoes, casein, alfalfa, carrot tops, soy-bean oil, pig, dog and beef liver, chestnut leaves, oat shoots, hemp seed and putrefied fish meal; also products of metabolism of certain bacteria, e.g., *Bacillus tubercle*, *Bacillus coli* and *Staphylococcus aureus*.

#### MODE OF ADMINISTRATION

Natural vitamin K concentrates may be given by mouth or intramuscularly in oily solutions. If given by mouth, bile salts must be administered simultaneously to insure adequate assimilation.

The synthesis of vitamin K active substances has almost entirely supplanted the use of the natural vitamin and for obviously good reasons. The synthetic compounds are all water-soluble in varying degrees and can be administered orally, subcutaneously, intramuscularly, intraperitoneally and intravenously without bile

salts. Intravenous administration produces a marked response in a few hours whereas the other routes may take twelve to twenty-four hours.

The average dose of 2-methyl-1, 4-naphthoquinone is 1 to 3 mg. daily. Much larger doses, however, can be given with safety if indicated. It is supplied in 1 mg. tablets and in oil solutions for oral use. It is not as water-soluble as other synthetic quinones. At the present time there are numerous vitamin K-active products on the market suitable for parenteral administration.

It is common practice now in some obstetrical centers to prescribe routine prophylactic doses of vitamin K to mothers in the form of 1 mg. tablets weekly during the last month of pregnancy and 1 mg. daily for the last two to three days antepartum. In addition, from 0.35 to 1 mg. daily doses of vitamin K are given to infants in the first week or two after birth.

*Vitamin K and Transfusions (Bank Blood).* It is important to bear in mind that the prothrombin concentration of bank blood diminishes rapidly after the third day and is practically useless as a source of prothrombin after the ninth day of storage.

#### TOXICITY

No toxic manifestations have been noted from tremendous doses of the natural vitamin K. Some anemia and general depression of the hematopoietic system has attended the use of very large doses of the synthetic products, including 2-methyl-1, 4-naphthoquinone. The therapeutic ratio, however, is so very high that one may use it without hesitation in the recommended clinical doses.

#### SUMMARY

Although the exact mechanism of blood coagulation is not fully understood, it is generally accepted that prothrombin, thromboplastin and calcium interact to form thrombin which combines with fibrinogen to form fibrin. The only physiological

anticoagulant known is heparin, which is not found in circulating blood in any appreciable amount.

Vitamin K apparently is a precursor or possibly an enzyme in the formation of prothrombin, which is a product of liver metabolism. Absorption of the natural fat-soluble vitamin K from the intestinal tract requires the presence of adequate bile salts and a normal intestinal mucosa. Its utilization after assimilation depends on the presence of healthy liver tissue for the formation of prothrombin.

Synthetic vitamin K products, generally more potent than the natural vitamin, are naphthoquinone derivatives, most of which are water-soluble and can be administered parenterally.

Vitamin K is of greatest value in correcting the abnormal blood coagulation due to hypoprothrombinemia as a result of obstructive jaundice or biliary fistulas. It is also useful in correcting hypoprothrombinemia of the newborn.

All patients submitted to biliary tract surgery in the presence or absence of jaundice should have prothrombin determinations and vitamin K therapy preoperatively and postoperatively. The plasma prothrombin response to vitamin K therapy in the presence of a hypoprothrombinemia may be used as a sensitive liver function test.

In the recommended therapeutic doses vitamin K and its related synthetic products are not toxic.

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THIS (generalized polyneuritis) may be brought about by vitamin deficiency, chemical poisoning, virus infection, or bacterotoxic agent.

# SULFATHIAZOLE IN THE TREATMENT OF APPENDICEAL PERITONITIS\*

A. F. JONAS, JR., M.D.

Instructor in Surgery, University of Nebraska

OMAHA, NEBRASKA

THE introduction of chemotherapy has stimulated great interest in the possibility of treating various forms of peritonitis with the sulfonamide agents. The report of Ravdin, Rhoads, and Lockwood<sup>1</sup> on the sulfanilamide treatment of appendiceal peritonitis is in point.

In the fall of 1939 we began to treat occasional cases of widespread peritonitis or peritoneal contamination with sulfathiazole. These cases, chiefly multiple gunshot wounds of the colon and perforated peptic ulcers of long duration, did so well clinically that we started the occasional use of the drug in cases of peritonitis due to perforated appendicitis. Since March 1, 1940, every patient having perforation of the appendix has promptly received sulfathiazole treatment. When possible the drug has been given by mouth—for adults of average size an initial dose of 4 Gm. followed by 1 Gm. every four hours. When complications such as vomiting or when the use of duodenal suction have prevented oral administration, the sodium salt has been given intravenously—for adults an initial dose of 4 Gm. followed by 2 Gm. every eight hours. Due to rapid excretion of the drug and to individual variations in excretion, frequent blood level determinations have been made and the dose tempered so as to maintain a level of 6 to 10 mg. per cent. Most of the patients have shown crystals of sulfathiazole in their urines but this has constituted no contraindication to continuation of therapy. A few patients have developed transitory oliguria or anuria with elevation of the blood non-protein nitrogen, but these manifestations have cleared in every case within thirty-six

hours of onset and following the liberal administration of intravenous glucose and saline.

Cultures from the cases here reported were invariably positive for one or more of the following organisms: most commonly Escherichia coli, aerobic and anaerobic streptococci, staphylococci, pneumococci, Bacillus welchii, and diphtheroids. Long and Bliss<sup>2</sup> have published observations on the bacteriostatic effect of sulfanilamide, sulfapyridine, and sulfathiazole on various bacteria *in vitro*. They found sulfathiazole to be slightly more effective than sulfapyridine against Escherichia coli while both drugs were much more bacteriostatic than sulfanilamide which exerted little or no effect. Klinefelter<sup>3</sup> has carried this inquiry farther by treating experimental Escherichia coli peritonitis in mice with these drugs. In twenty-five control mice the mortality was 100 per cent, in twenty-five mice treated with sulfanilamide the mortality was 96 per cent, in twenty-five mice treated with sulfapyridine the mortality was 0 per cent, and in twenty-five mice treated with sulfathiazole, only 4 per cent.

During the period from March 1, 1940, to May 1, 1941, we have treated sixty-one patients with perforated appendix associated with abscess or peritonitis with sulfathiazole. In every case the appendix was removed and the abdomen drained. In no instance was the drug placed directly in the peritoneal cavity; such practice makes it very difficult to control toxic reactions when they occur. Since the mortality from nonperforated appendices is negligible, no such cases are included in this report although the inclusion of some

\* From the Department of Surgery, Johns Hopkins Hospital and University, Baltimore, Maryland.

200 concurrent cases of this sort would color favorably the mortality rate. In no other detail than the use of sulfathiazole has the treatment differed from that reported by Stafford and Sprong<sup>4</sup> from this hospital. In their series of 479 similar cases occurring during the preceding eight years, there were forty-eight deaths, yielding a mortality rate of 10.02 per cent. In the current series of sixty-one cases, there were two fatalities, a gross mortality of 3.28 per cent. One of these patients, a negro boy of 12 years, came to the hospital on the ninth day of his illness with advanced generalized peritonitis. He died after a prolonged course of eight weeks during which several additional operations were done for subphrenic abscess, pelvic abscess and empyema. At autopsy he showed at least five distinct abdominal abscesses lying chiefly along the root of the mesentery and between loops of intestine. The other fatality occurred in a white woman who reached the hospital on the fifth day following perforation. She seemed nearly moribund but operation was performed under local anesthesia, her appendix re-

moved and her peritonitis drained. She died five hours after operation but since she received one intravenous dose of sulfathiazole, must rightfully be included in this report. Were she not, the gross mortality would be 1.64 per cent.

Since sulfathiazole is the least toxic of the three sulfonamides in common use and also has the widest range of activity, it is logical and successful, too, to employ it in the treatment of peritonitis of appendiceal origin. Its value in the treatment of concomitant postoperative pneumonia is an additional reason for its use.

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# OVARIAN LESIONS SIMULATING APPENDICITIS\*

EDWARD F. McLAUGHLIN, M.D.

Surgeon, Nazareth Hospital

PHILADELPHIA, PENNSYLVANIA

THE ovarian lesions which most often give symptoms suggestive of appendicitis are ruptured Graafian follicles, follicle and corpus luteum cysts and bleeding corpora lutea. The syndrome that is set up is of fairly frequent occurrence; the possibility of its occurrence is even more likely, since a slight deviation from the normal physiological changes of any menstrual cycle may give rise to it.

Excessive hemorrhage from a normally rupturing follicle at the time of ovulation probably accounts for the mid-period type of pain—the mittel-schmerz. Bleeding from an insecurely “plugged” corpus luteum or the rupture of a cystic corpus luteum is the commonest type and occurs usually between the time of ovulation and of menstruation. Breaking of the more established so-called simple cysts which may have arisen from atretic follicles or persistent corpora lutea also gives rise to symptoms of appendicitis and may occur at any time in the menstrual cycle. The peritoneum is irritated in any of these instances by the escaping blood. Perhaps it is irritated at times by the cystic fluid. The reaction is mild—an active hyperemia—although at times some true inflammatory changes have been noted.

The number of reported cases of this “disease” is small. Articles by Hoyt and Meigs<sup>1</sup> Manizade,<sup>2</sup> Sexton,<sup>3</sup> Harris and Groper,<sup>4</sup> Weil,<sup>5</sup> McLaughlin,<sup>6</sup> Guy and Rotundi,<sup>7</sup> and Castallo<sup>8</sup> cover the field fairly well as far as literature on the subject goes. It is deemed worth-while, therefore, to report some additional cases, to discuss their relation to appendicitis and to evaluate the results of operative treatment in preventing further attacks.

## PRESENT STUDY

Forty nine patients\* with ovarian lesions simulating appendicitis were studied. Eight were nonoperative cases (Case I†). Seventeen showed unruptured cysts at operation (Case II). (In this second group it is believed that cyst ruptures had occurred previously but operation happened to come at the end of an attack or in an “interval stage.”) In three more both appendicitis and cyst rupture existed simultaneously (Case III). The remaining twenty-one cases showed freshly ruptured cysts of the ovary (Case IV).

All patients were white. The white predominance, evident in other reports as well as this, is so constant that one may almost say the condition is limited to white women. The patients’ ages varied from thirteen to forty-two, the average being 24.3; 69.3 per cent of the women were single.

*Symptoms and Signs.* The symptoms and signs of cyst rupture follow in sequence the pathologic happenings in the abdomen and are in direct proportion to their severity. They arise from (1) the local irritation caused by the escaping blood or cyst fluid; this gives rise to most symptoms; (2) the irritation of more distant areas of peritoneum as when the escaped fluid makes its way to the upper abdomen or under the diaphragm; (3) possibly by visceral response to the irritation of its

\* The patients studied, other than the author’s, were under the care of several different Philadelphia surgeons; Doctors W. B. Swartley, C. F. Mitehell, W. E. Lee, E. B. Hodge, S. D. Weeder, R. Alston and J. Toland, who have kindly permitted the use of their case histories.

† Case histories illustrating the four types of patients will be found at the end of the paper.

\* Read before the April Meeting, 1941, of the Philadelphia Academy of Surgery.

covering peritoneum, and (4) again possibly by absorption through the peritoneum of hormones from the escaped fluid or from an underlying etiologic hormonal stimulus itself. This hormonal stimulus, whatever be its source, accounts for the spotting which occurs in some of the cases (12 per cent).

It may also make a woman more sensitive to pain stimuli as is described in the related state of "premenstrual tension."

Among the signs and symptoms we find that pain, mild but definite, was common to all but one patient and was located in the lower right quadrant in 69 per cent of instances. It was never in the lower left quadrant alone, but was "abdominal" four times and epigastric five times. In but 18 per cent of the cases, did the onset resemble the generalized onset of acute appendicitis pain. Nausea was experienced by about half the patients (54 per cent) while only 19 per cent vomited. Lower right quadrant tenderness accompanied the other symptoms 96 per cent of the time but rigidity could be demonstrated in just 13 per cent of the examinations. The tenderness could only be gotten on so-called "deep" palpation in 20 per cent of the cases. One finds that the onset of symptoms was sudden in twenty-two cases (45 per cent) and slow in twenty-seven (55 per cent). They began on the average 16.9 days after the onset of the preceding period and 10.9 days before the next one started. There was a semblance of regularity to the recurrence of attacks in but eleven patients (22 per cent) while thirty-five (71.4 per cent) had had previous regular or irregular attacks; the classical regularity of the Mittle-schmerz was not very evident. All but six of the patients (12 per cent) had regular menstrual periods (88 per cent).

The record of temperature, pulse, leucocyte count and polymorphonuclear percentage is best expressed in Table 1. In a word, these values in all our ordinary cases were at the high level of normal. In the three cases in which acute appendicitis was associated with the ovarian lesion, the

average values were temperature 100.2° F., pulse 119, white blood count 16,900, polymorphonuclears 79.5 per cent—much higher than in the general group.

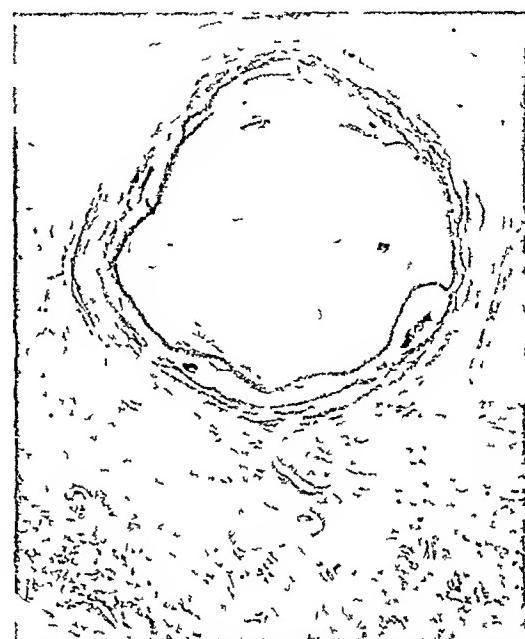


FIG. 1. Graafian follicle bulging from ovarian surface; ovarian tissue over follicle thinning out in preparation for rupture.

Examination of the pelvis by rectum or vagina was not done in two-thirds of the cases (65.3 per cent), a valuable maneuver having thus been omitted. When it was done (seventeen times) tenderness was revealed ten times and cystic ovaries were palpated three times.

*Diagnosis.* Appendicitis was considered as a diagnosis in all the cases. It was first choice in 56.6 per cent and secondary in 43.4 per cent. Ovarian lesions were considered as an underlying cause 77 per cent of the time and were the primary diagnosis in 41 per cent of cases. In two of the three cases of appendicitis with associated cyst rupture both conditions were considered preoperatively.

*Operative Findings.* In the forty-one patients operated upon, ruptured cysts were found twenty-one times (51 per cent), unruptured cysts in seventeen (41 per cent) and ruptured cysts plus acute appendicitis in three (7.5 per cent). The left ovary was

involved seven times (17 per cent), the right ovary thirty-one times (73 per cent), both ovaries once and in one instance the

## DISCUSSION

*Differential Diagnosis.* Ovarian follicles and simple cysts probably come and go



FIG. 2. Section at site of a rupture. The surface covering has gotten down to an almost one-layer thickness. Early luteinization of lining cells has begun.

ovary involved was not designated. Old blood, or bloody fluid was found in nineteen cases (46.3 per cent). In some of the others there seemed to be an amount of clear fluid greater than normal. Adhesions were noted in four cases (7.9 per cent); in one instance these adhesions blocked the tubes.

TABLE I  
AVERAGE VALUES FOR THE ITEMS LISTED IN THE  
DIFFERENT GROUPS OF GASES STUDIED

	Temper- ature °F.	Pulse	Leuco- cytes	Poly- morpho- nuclears
Total .	98.8	89	10,500	71.7
Ruptured cyst	98.8	89	9,700	71.4
Cystic ovaries	98.6	86	10,700	69.6
Nonoperative	98.5	85	10,600	76.2

36 per cent had counts of 10,000 or over.  
34 per cent had temperatures of 99°F. or more.

*Operative Treatment.* Appendectomy was done on all the operated patients. Partial oophorectomy with oversewing was done in thirty-seven (90 per cent). Oophorectomy was performed three times (7.5 per cent) and salpingo-oophorectomy once (2.5 per cent). There was no mortality in the present group.



FIG. 3. Early corpus luteum showing hematoma-like center. This had blown out its "plug" and was found bleeding at operation.

without giving any appreciable symptoms 90 per cent of the time. When they do cause trouble, it often resembles appendicitis so closely that any thought of delaying operation would be folly. Yet on the other hand, in many instances there are recognizable differences and if these are carefully weighed, the diagnosis of the ovarian lesion can be made with a sufficient degree of accuracy and a nonoperative course pursued. In general the differences can best be expressed by tables. Table II shows the main differences from acute appendicitis and Table III those from recurrent appendicitis.

TABLE II  
ESSENTIAL DIFFERENCES BETWEEN CYSTS AND ACUTE  
APPENDICITIS

Acute Appendicitis	Ruptured Cyst
1. Pain general, later localizing	Pain local and remains so
2. Nausea and vomiting	Nausea less frequently; vomiting unusual
3. No discharge	Spotting occasionally
4. Tenderness, definite McBurney's	Tenderness slight; lower
5. Rigidity	Absence of rigidity
6. Temperature and pulse elevated	Temperature and pulse normal
7. White blood cells and polymorphonuclears increased	White blood cells and polymorphonuclears about high normal

*Acute Appendicitis.* From acute appendicitis the points of difference are essen-

tially as follows: The onset in acute appendicitis is usually gradual and general, later localizing in the lower right quadrant. The onset in the kind of cyst cases comparable to acute appendicitis is often sudden. But sudden or slow it almost invariably begins as a localized pain and remains so or becomes more generalized later. Tenderness is much more acute in appendicitis and one does not need to do a "deep" palpation to get it. It centers roughly around McBurney's point. Tenderness in cyst rupture is absent or of a mild degree. It is not definitely centered but is found lower down than in appendicitis. One does not often get rigidity after cyst breaking; nausea occurs occasionally and vomiting almost never. In contrast, the usual history of acute appendicitis contains a record of both nausea and vomiting following the onset of pain. Fever, pulse rise, leucocytosis and increase in percentage of polymorphonuclear cells characterize appendicitis. In the other cases one often finds a normal temperature and pulse rate or perhaps a slight rise above normal and the white cells and the differential count are usually at high normal limits.

TABLE III

## DIFFERENTIAL POINTS IN CYST RUPTURE AND RECURRENT APPENDICITIS

Recurrent Appendicitis	Ruptured Cyst
1. Irregularity of occurrence	Sometimes regular
2. Unrelated to menstrual cycle	Mid-period or latter half of cycle
3. Right side	Occasional left sided attack
4. No discharge	Spotting or discharge with attack
5. Occasional acute attacks	No typical appendical attack
6. No masses	"Phantom" tumor

*Pelvic Appendicitis.* A very dangerous condition in any case, pelvic appendicitis may be said to mask itself by simulating ovarian disease rather than the reverse. For too long a time the initial signs and symptoms, mild enough to suggest very strongly a cyst rupture, will persist in their mildness because of the pelvic location of the appendix and the distinguishing points

of rigidity, fever, tachycardia, leucocytosis, etc., may appear only after appendiceal rupture has taken place. The pelvic findings of tenderness and possibly a small mass are almost useless. It may be said that the patient with appendicitis is distinctly the sicker one, but this will not make the differential diagnosis. The obvious answer is that one should operate if there be any reasonable suspicion of appendicitis existing in the pelvis.

*Chronic or Recurrent Appendicitis.* In this type of appendicitis and in those cases of cystic disease resembling it, symptoms are mild and immediate decision as to operation is not imperative so that one may take more time to arrive at an accurate differential diagnosis. In this group of cases accurate differentiation is possible if one has the patience to study them over a sufficient period of time, that is, through several menstrual cycles. First, an accurate history is important. The woman patient is rare who will volunteer any information as to when her attacks of pain have come in relation to the menstrual cycle. She does not think of them in that light and neither do many physicians. If it can be elicited that they come with a fair degree of regularity at mid-period time (halfway between menses), a very valuable clue has been gotten as to their source. Most cases of cystic rupture do not have this characteristic of regularity, however. But most patients will give the history that their attacks occasionally shift to the left side (if one keeps the patient under observation long enough to find this out). While it is true that rupture of cysts in the left ovary frequently give rise to right-sided symptoms, yet there will certainly be some attacks entirely centering in the lower left quadrant.

The occurrence of mid-period spotting accompanying lower abdominal pain is about the most pathognomonic sign of follicle cyst rupture. It is a very helpful symptom when it occurs but it is recorded rather infrequently (12 per cent of present cases). In some patients there occurs a

whitish, or yellowish, or even watery discharge with their pain but this is usually overlooked and only of slight value in differentiation if present.

Recurrent appendicitis is in reality a succession of mild attacks of acute appendicitis so we should expect the exhibition of fairly classical symptoms during some one attack. Certainly the chance that temperature, pulse and leucocyte count will be higher is much greater than in the ovarian conditions. Nausea and vomiting are, of course, more likely to occur when the appendix is involved.

Curtis has described what he calls the "phantom tumor," a simple cyst of the ovary which ruptures between examinations, so that in successive examinations no sign of the previously described pelvic mass can be felt. This point can be made use of in a patient suspected of having recurrent pain from cyst rupture, by having her report for a pelvic examination every few days through a menstrual cycle. The examinations may reveal that one ovary enlarges before her attack of pain occurs and is decreased in size afterward.

*Diagnosis at Operation.* Since the existence of a ruptured cyst is so often either not considered or only secondarily thought of, one must say a word about the identification of such a condition when the abdomen is opened. First, it is probably true that in many instances ruptured retention cysts are overlooked through failure to examine the pelvis or by making a very cursory pelvic examination, not visualizing the ovaries. Through a McBurney incision it is difficult accurately to feel both ovaries and it is almost impossible to expose the left one. Through a small or high right rectus incision it is again difficult truly to appraise the pelvic viscera. At times an appendix, whose outer coat is hyperemic due to the irritating fluid in the peritoneal cavity, is taken to be the sole source of trouble, is removed and the abdomen closed. Ignorance is bliss in such a case until the patient returns a few months later wanting to know why attacks

of pain similar to those suffered preoperatively are coming back just as often and just as severely.

Upon opening the peritoneal cavity one may find nothing abnormal. Even the ovaries may seem within normal limits. Closer inspection may reveal a small cyst that has a dark spot on its surface as the only remains of an opening through which fluid escaped. These are the cases in which the patients symptoms have been present for some days and by the time of actual operation the "evidence" may be gone.

At the other extreme, one may open the abdomen and find definite hemorrhage and an increased volume of intra-abdominal fluid. The visceral surfaces may appear injected but I have never seen the process advanced to a degree where plastic exudate was found. The ovary may show a cyst wall with a rent in it. There may be a persistent trickle of blood from this or the opening may be sealed over with a clot. Some cysts will be filled with blood and have a plug of coagulated material in a small round hole on the surface. At times blood has been seen coming past the edges where such a plug was not tight. At a later stage one may find the cyst closed and shrunken with only a few small clots of blood in the pelvis to indicate what has taken place.

*Postoperative Diagnosis.* Even with a ruptured cyst oversewn, the appendix, incidentally removed, and the abdomen closed one is not yet able to rest on his diagnosis. For the obliging pathologist often reports "low grade appendicitis," "fibrous appendicitis," etc., with "fragments of ovarian tissue resembling corpus luteum." The more convenient diagnosis of "appendicitis" is used in the record room and another case of cyst rupture which was taken for appendicitis and which led to a laparotomy not absolutely necessary, is effectively buried.

*Treatment.* It is believed from the data presented that there are those cases which can be safely and with a sufficient degree of accuracy distinguished from appendicitis.

If a diagnosis of the ruptured cyst syndrome can be made, no operative treatment is indicated unless the symptoms prove too distressing or if there is evidence of too much blood loss. It is well to remember, however, that once a patient is put down as suffering from the ovarian cyst rupture syndrome every attack of abdominal pain, especially that localizing in the lower right quadrant, is not assuredly from this same cause. Such a patient should be examined in each attack to eliminate if possible the question of appendicitis. One such patient appeared in our series in which after repeated attacks of intermenstrual pain, one attack differed from the others. Operation was done and an acute appendicitis was found associated with a leaking corpus luteum cyst.

Where there is a reasonable doubt as to whether or not a given patient suffers from appendicitis or cyst rupture, let it be clearly understood that operation is mandatory.

#### FOLLOW-UP

The immediate problem is solved by operative removal of the leaking cysts. But the underlying urge remains. There is no assurance that the lesion will not again arise in the same or the opposite ovary. However, the main question is: "How often do clinical symptoms recur?" In searching for an answer twenty-eight of the thirty-one eligible operative patients in this series were followed and 78.8 per cent had no recurrence. The literature furnishes little help on this point and so letters were addressed to men interested in the subject. Meigs<sup>9</sup> recalls no patient, to whom the situation was properly explained, coming back with the same complaint unremedied. Guy<sup>10</sup> recalls but three or four patients who had symptoms persist after operation. Weil<sup>11</sup> had nine cases recur out of fifteen followed. Castallo<sup>12</sup> tells of four personal cases with no recurrences. Harris<sup>13</sup> had recurrences in but two of fifty cases and believes that "the operative resection of organized corpus luteum or follicle cyst from the ovary is practically a cure" and

thinks there is a higher incidence of recurrence in nonoperated patients. Totaling all the available figures (Table IV), we may say that 82 per cent of ninety-seven cases showed no return of clinical symptoms which could be attributed to a repetition of the cyst rupture syndrome. This is comforting to the conscientious surgeon who finds no acute appendicitis upon opening an abdomen but a ruptured cyst and who often wonders whether he is doing the patient any good by resecting the cyst which is the immediate offender. It would seem from the figures collected that the patient was being distinctly benefitted by the cyst removal.

#### CASE REPORTS

CASE I. M. McH., No. 49, came home from work with a persistent pain in the lower right side, fearing she had appendicitis. She had had previous attacks during the few months preceding, each time shortly before a menstrual period. The present attack began twelve days before the expected period and was accompanied by some spotting of blood. Her temperature was 98.6°F., and pulse 72. Tenderness in lower right quadrant was practically nil. She was observed for twenty-four hours, by which time symptoms had subsided.

CASE II. D. W., No. 37, a woman of twenty-five had about six attacks of lower right quadrant pain which gave symptoms for a day or so. These usually came near mid-period or in the early part of the latter half of the cycle. Usually no fever accompanied the pain. The patient desired to have "something done" and operation was performed away from the time of an attack. Unruptured retention cysts of both ovaries were found and excised; the appendix was normal.

CASE III. M. B., No. 20, nineteen years of age, had sudden pain in the right lower quadrant while stepping into a car. Her period was due in ten days. Within three hours she was hospitalized and there was tenderness but no rigidity in the lower right quadrant. She was nauseated and vomited. Her temperature was 100°F., pulse 120, white blood cells 19,400, polymorphonuclears 78. Cyst rupture was suspected and she was allowed to go till morning when operation was thought advisable with

tenderness still persisting. A ruptured cyst and an acute pelvic appendix were found.

CASE IV. I. G., No. 8, a nurse of twenty, at mid-period time had a sudden pain in the lower right quadrant. It remained localized to that area. There was no nausea or vomiting. Her temperature was 98.2°F., pulse 92, white blood cells 8,400, polymorphonuclears 84. Tenderness and some rigidity were noted in palpating the lower right quadrant of the abdomen. Operation was advised to be on the safe side and upon opening the abdomen blood-tinged fluid was seen and a small oozing cyst of the right ovary exposed. The cyst was resected, the exposed ovarian tissue oversewn and the appendix removed.

#### SUMMARY AND CONCLUSIONS

1. The ovarian lesions which most often simulate appendicitis are ruptured follicles, follicle and corpus luteum cysts and bleeding corpora lutea. Forty-nine such cases are reported.

2. A certain number of these may be clinically differentiated from appendicitis and a nonoperative course pursued.

TABLE IV  
RESULTS OF FOLLOW-UP STUDIES ON CYST RUPTURE CASES

	Cases	Recur- rences	Symp- tom Free	Cure, Per Cent
Harris.....	50	2	48	96
Weil.....	15	9	6	40
Castallo.....	4	0	4	100
Present series.....	28	6	22	78.6
Total.....	97	17	80	82

#### NON-OPERATIVE

Patient	Number	Date	Hospital
C. S.....	Private Patient		
M. McL.....	Private Patient		
E. M.....			
I. S.....		4-4-41	Municipal
M. F.....		4-14-41	Municipal
C. Y.....		4-8-41	Municipal
F. B.....	12104 Private Patient	10-28-40	Germantown
M. McH.....	Private Patient		

TABLE IV—(Continued)  
CYSTIC OVARIES

Patient	Number	Date	Hospital
D. S.....	35928	10-1-39	Germantown
V. K.....	25830	2-8-39	Germantown
M. D.....	33785	3-22-39	Germantown
M. P.....	40154	10-8-40	Germantown
G. S.....	35245	7-29-39	Germantown
E. McE.....	35615	9-4-39	Germantown
C. H.....	32952	1-2-39	Germantown
R. B.....	36295	11-4-39	Germantown
D. R.....	35980	10-6-39	Germantown
M. F.....	36567	11-30-39	Germantown
A. M.....	25541	4-26-40	Germantown
D. S.....	1803	2-26-41	Nazareth
D. W.....	1756	2-19-41	Nazareth
R. S.....	323	5-31-40	Nazareth
G. M.....	421	6-20-40	Nazareth
H. B.....	256	5-15-40	Nazareth
G. K.....	214	5-5-40	Nazareth

#### RUPTURED CYSTS

Patient	Number	Date	Hospital
E. H.....	10349	10-12-39	Chestnut Hill
L. N.....	10350	3-23-39	Chestnut Hill
C. McK.....	32582	11-22-38	Germantown
N. B.....	5540	12-31-38	Chestnut Hill
M. G.....	11631	9-19-40	Chestnut Hill
F. E. E.....	35835	10-3-39	Germantown
W. O'D.....	34469	5-25-39	Germantown
I. G.....	28942	3-22-39	Germantown
M. R.....	35296	8-3-39	Germantown
T. N.....	23682	9-16-36	Germantown
A. G.....	21062	10-11-39	Germantown
C. McG.....	36135	10-21-39	Germantown
V. F.....	35656	9-7-39	Germantown
J. S.....	35793	9-19-39	Germantown
A. G.....	5161	4-12-40	Germantown
M. B.....	33360	2-1-40	Germantown
M. C.....	36283	11-2-39	Germantown
R. L.....	32936	1-1-39	Germantown
K. McC.....	28623	1-3-41	Germantown
M. B.....	10076	9-7-39	Chestnut Hill
G. G.....	1662	2-1-41	Nazareth
S. C.....	1703	2-15-41	Nazareth
R. D.....	1947	3-20-41	Nazareth
E. B.....	1877	3-13-41	Nazareth

3. If the ovarian lesions be found when the abdomen is opened, resection of the cystic portion will give freedom from further clinical symptoms in 82 per cent of cases.

4. The final word should be an admonition not to hesitate to open the abdomen

in those cases in which any doubt exists as to the possibility of appendicitis.

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TUMOR of the ovary may be solid or cystic, benign or malignant, small or huge. Primary ovarian tumor can occur at any time: before puberty, during menstrual life, or after menopause. Metastatic tumor of an ovary is not uncommon, especially from the gastro-intestinal tract, breast, cervix, or uterus.

# THE PRINCIPLES OF SURGICAL TECHNIC\*

WITH COMPARISON OF RESULTS OBTAINED WITH FINE SILK, FINE CHROMIC CATGUT AND LARGE CATGUT (CHROMIC AND PLAIN)

LIEUT. COMDR. CHARLES H. LUPTON, M.C., U.S.N.R.

Surgeon, Norfolk Naval Hospital

NORFOLK, VIRGINIA

THE purpose of this article is to stress the importance of observing certain well defined principles of surgical technic, and to make a comparison of the results obtained when using (1) *fine silk*, (2) *fine chromic catgut*, and (3) *large catgut* (chromic and plain).

This series consists of 400 unselected and consecutive cases in which the peritoneal cavity was opened. There are 125 consecutive patients in each of the *fine silk* and *large catgut* (chromic and plain) groups, and 150 consecutive patients in the *fine chromic catgut* group.

The instructions given to the interns on the use of and the clinical investigation of *fine chromic catgut*\* were as follows:

1. This investigation is being conducted to determine: (a) If as satisfactory results could be obtained when using *fine chromic catgut* as were obtained when using *fine silk*;† and (b) to make a comparison between the results obtained when using *fine chromic catgut* with a refined technic, and *large catgut* (chromic and plain) as ordinarily used.

2. The skin, subcutaneous tissues, muscles and fascia must be completely covered with laparotomy pads or towels immediately after making the incision, and they should be kept covered until they are ready to be closed. After the peritoneum is opened the moist laparotomy pads or towels should be attached to it.

\* From the surgical services of the Norfolk General Hospital and Norfolk Naval Hospital.

† Principles of surgical technique with particular reference to the use of silk. *Am. J. Surg.*, 45: 309-315, 1939.

3. Small hemostats, small forceps, small needles and small needle holders should be used.

4. The inclusion of large amounts of tissue when ligating and transfixing bleeders should be avoided.

5. Careful hemostasis is one of the most important factors in avoiding postoperative complications.

6. It is suggested that the following sizes of *fine chromic catgut* be used: (a) No. 0000 should be used for ligating and transfixing small vessels. (b) No. 000 should be used for ligating a moderately sized vessel. (c) When a moderately large or a large vessel is to be ligated, use No. 00 or No. 0. (d) For closing the peritoneum and transversalis fascia, No. 0 is advisable. (e) For suturing muscle No. 0000 or No. 000 should be used. (f) For closure of fascia use No. 0, except in long upper abdominal incisions or where there is much tension it may be necessary to use No. 1. (g) Under no circumstances should a size larger than No. 1 be used for any purpose. (h) Only the *fine chromic catgut* which has been furnished by one manufacturer will be used in this investigation.

7. A square knot should be used for the majority of ligatures of small vessels, but for larger vessels a surgeon's knot or a triple throw knot tied square will be necessary, the latter being preferable to the surgeon's knot when using catgut. "Granny knots" must be avoided. The sutures should be cut closer to the knot than they would if *large catgut* were used, but the length of the suture from the knot should

\* Read before the Seaboard Medical Association (N. C. and Va.), December 3, 1941. The opinions expressed in this article are those of the writer and are not to be construed as reflecting the views of the Navy Department.

depend upon the size of the suture, the tension it is under and the importance of the knot.

8. Records of maximum postoperative temperatures, evidences of infections or disturbances of primary healing, estimation of the amount of abdominal distention and the general condition of the patients should be carefully made.

9. *Infections.* (a) Whenever there is any disturbance of primary union, it should be recorded. (b) Serum suggests minor infection. (c) Pus indicates major infection. State whether slight, moderate or severe.

The same technic was attempted in both the fine silk and fine chromic catgut groups; however, in the large catgut (chromic and plain) group, there was not as much refinement of technic in regard to the use of small hemostats, small needles, clamping small amounts of tissue, keeping the edges of the wound covered while operating, etc. In other words, the technic in the large catgut group was similar to that employed by the average surgeon using large catgut.

It should be the aim of the surgeon to improve his technic, not only in order to secure more recoveries, but also to lower his morbidity rate. The surgeon's knowledge of the principles of surgical technic, as well as his surgical philosophy, will be indicated by his percentage of infections in clean surgical cases, and by the incidence of low postoperative temperatures with resultant low morbidity and low mortality rates.

The teachings of Dr. Elliott C. Cutler and Dr. Robert Zollinger have been a stimulus toward the development of a more refined surgical technic. The result has been a lower morbidity rate with fewer complications; therefore, the postoperative care has not played so important a rôle as it did previously.

In order to re-emphasize the importance of (1) complete examination of the patient, (2) adequate preoperative preparation, and (3) a more refined surgical technic, I wish to repeat a statement made in a previous

article.\* "There has been voluminous literature during the past two decades or more on the importance of preoperative preparation and postoperative care. I do not desire in any way to detract from the importance of all that has been written; in fact, I think it would be well to re-emphasize and concur in the importance of careful preoperative and postoperative measures. But this point I do wish to make: if there has been proper preoperative investigation and preparation, and a careful technique—including gentleness and careful hemostasis during the operation—then there will be fewer postoperative complications, and the postoperative care will not play so important a part."

#### LOW POSTOPERATIVE TEMPERATURES

The significance of low postoperative temperatures should be re-emphasized. It is surprising to find so little literature on this subject. The one thing that usually has the most significant meaning on the clinical record is the postoperative temperature. If this has remained low, it would certainly be reasonable to assume that no serious complication had arisen, eliminating emboli and allied conditions. The more refined the surgical technic, the lower will be the postoperative temperature and the morbidity rate.

The factors in producing low postoperative temperatures and more satisfactory postoperative courses are: (1) asepsis and certain measures employed to minimize wound infections; (2) careful hemostasis; (3) gentleness, and (4) correct use of proper suture material.

#### ASEPSIS AND CERTAIN MEASURES EMPLOYED TO MINIMIZE WOUND INFECTION

Every surgeon attempts to use an aseptic technic. This has been emphasized so much, and its importance is so well known to surgeons everywhere, that it seems needless to discuss this subject again, except to

\* Am. J. Surg., 45: 309-315, 1939.

re-emphasize that the surgeon must be constantly on guard to make certain that there will be no break in the aseptic technic.

Many measures are employed to minimize wound infections. I have not attempted to list all of those measures, in fact I have listed only those measures, most of which are part of the aseptic technic which I wish to emphasize because they are not always strictly observed. In discussing *certain measures employed to minimize wound infections* it is realized that these measures are employed by the vast majority of surgeons. It is only because some surgeons do not employ all of them or are somewhat careless in their employment, that it seems necessary to stress certain phases of their importance here.

*A. Adequate Sterilization of the Hands and Arms of the Operative Team.* The adequate sterilization of the hands and arms of the surgeon and of the operative team is a most important part of aseptic technic. It is impossible completely to sterilize the hands and arms for more than a short period of time even with the best methods in use. Some methods which are thought to be satisfactory do not completely sterilize the surface of the skin for even a short period. In other words, positive cultures will be obtained in many cases when cultures are taken immediately from the nails, after manicuring the nails, scrubbing the hands and arms with soap and water for ten minutes and then immersing the hands and arms in one basin of alcohol (70 per cent). If immersions in two separate basins of alcohol are made, the percentages of positive cultures will be very much reduced. During a time when there was an epidemic of acute respiratory infections, using the method of preparation described above in a small series of cases the following results were obtained:

After using alcohol (70 per cent), 100 per cent of the cultures were positive; after using two separate basins of alcohol (70 per cent), 10 per cent of the cultures were positive. When substituting an aqueous solu-

tion of zephiran (1-1000) for the alcohol, all cultures were negative. The more careful the manicuring of the nails and the scrubbing of the hands and arms, the lower the percentages of positive cultures will be, regardless of the antiseptic used. It is realized that when there are infections of the nose and throat of members of the operative team the percentage of positive cultures will necessarily be high, and it is also realized that no definite conclusions can be drawn from a small series of cultures; nevertheless from this limited experience an aqueous solution of zephiran (1-1000) for one minute, or a weaker solution of 1-3000 for three minutes appears to be a splendid antiseptic for the hands and arms. The stainless tincture of zephiran (1-1000) may be used for arm and hand soaks. It must be remembered that it is absolutely necessary to remove all soap before using zephiran. When using an aqueous solution of zephiran there is no drying or irritation of the skin; in fact, when using the wet-glove technic the hands are often in as good a condition after operating as they were before. The wet-glove technic, when using an aqueous solution of zephiran, is superior to the dry-glove technic.

*B. Adequate Sterilization of the Operative Field.* The operative area should be properly shaved and thoroughly cleansed with soap and water, taking care to remove all soap. When in the operating room, the operative area should first be cleansed with ether and alcohol. When a tincture of zephiran is used, make two applications and rub it gently into the skin of the operative area. The alternate rubbing of the skin of the operative area, first with an aqueous solution of zephiran (1-1000) and then with alcohol (70 per cent), using six sponges of each, beginning along the line of the proposed incision and working outward toward the periphery of the operative field, is one of the best methods of preparing the operative area.

*C. Proper Sterilization of Sutures, Instruments, Linen, Supplies, etc.* It is the

responsibility of the surgeon to see that all sutures, instruments, linen, supplies, etc., are properly sterilized. He should familiar-

nose and throat may harbor highly virulent organisms, particularly the hemolytic streptococcus or the hemolytic staphylo-

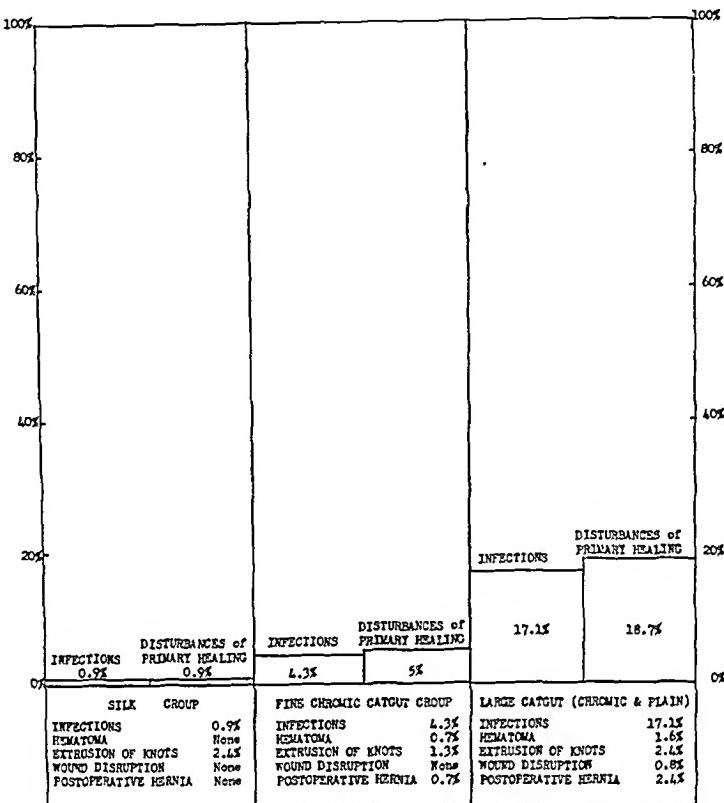


FIG. 1. Graph showing the comparison of infections, etc., in a series of fine silk, fine chromic catgut and large catgut (chromic and plain) cases.

ize himself with the improved methods of sterilization of instruments. Cultures should be made frequently from the supplies and instruments to be certain that adequate sterilization has been carried out.

While it has been proved by certain investigators that catgut was not always sterile, it is not believed that catgut is often a source of wound infection at the present time.

*D. Adequate Masks.* The average masks are not adequate for the purpose for which they are intended. They are not large enough to prevent the escape of moisture, neither do they completely filter all bacteria in the moisture from the nose and throats. It must be recognized that surgeons with equally refined technic may not always obtain similar results. One surgeon's

coccus aureus. Naturally, the surgeon who harbors those highly virulent organisms cannot obtain as satisfactory results as the surgeon who is not a carrier of such organisms. The nose and throat is a more frequent source of wound infections than is generally realized.

After using the various types of masks, including the "deflector types," it seems that the type of mask described by Dr. DeTakats and Dr. Jesser\* is the most efficient and satisfactory. This type of mask with a few minor changes has been used for a few months and it appears to be more suitable than any type previously used. It is made of one layer of Canton flannel 9 by 7½ inches (these dimensions should be reduced one-half inch for nurses), which is

\* *Surg. Gynec. & Obst.*, June, 1941.

placed between two layers of crinoline (discarded from adhesive plaster). It is sewed twice (one-half inch apart) around

source. However, agitation of floor dust should be avoided by the use of too vigorous air currents. Air-conditioning is to be

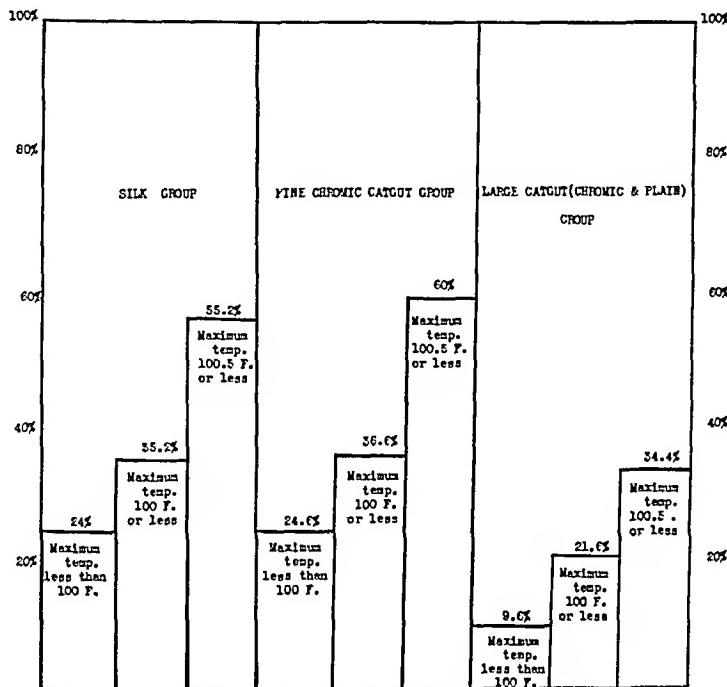


FIG. 2. Graph showing the comparison of low postoperative temperatures in a series of fine silk, fine chromic catgut and large catgut (chromic and plain) cases.

the edges, and then diagonally across from the corners to prevent the Canton flannel from rolling or becoming detached. Two three-fourth-inch tucks are taken at each of the ends, and two, three-eighth-inch tucks are taken at the bottom of the mask. A piece of one-half-inch tape, the length of the mask, is sewed along the upper border; then a piece of one-half-inch tape 40 inches long is sewed along each of the upper and lower borders of the mask. A small aluminum metal strip is inserted between the two pieces of tape along the upper border of the mask, the purpose of which is to make the mask fit around the nose and face. The mask is not tight across the mouth, although it fits well around the face.

*E. Air-Conditioning and Special Bactericidal Radiant Energy.* With the frequent change of air in the operating room, through air-conditioning, the number of organisms in the air is reduced, thereby lessening the danger of infection from this

especially recommended for the operating room in warm climates.

*Special Bactericidal Radiant Energy.* The attempted sterilization of the air in the operating room as recommended by Hart is believed to be of value, particularly when all other precautionary measures have been employed and infections are greater than ordinarily expected.

*F. Minimize External Sources of Infection after the Operation.* Many measures can be taken to minimize external sources of infection after the operation. The nose, mouth and throat of those doing dressings, adjacent patients, visitors, as well as the patient himself are often external sources of infection after the operation, particularly those infections occurring late. When late infections occur, all possible sources of infection should be investigated and eliminated if that is possible. Patients developing respiratory infections should be transferred from surgical wards promptly; when

that is not feasible, they should be isolated. Those having respiratory infections should not do dressings, but if for any reason they do, masks should be worn.

One of the important factors in preventing the development of postoperative pulmonary complications, particularly atelectasis, is adequate aeration of the lungs.

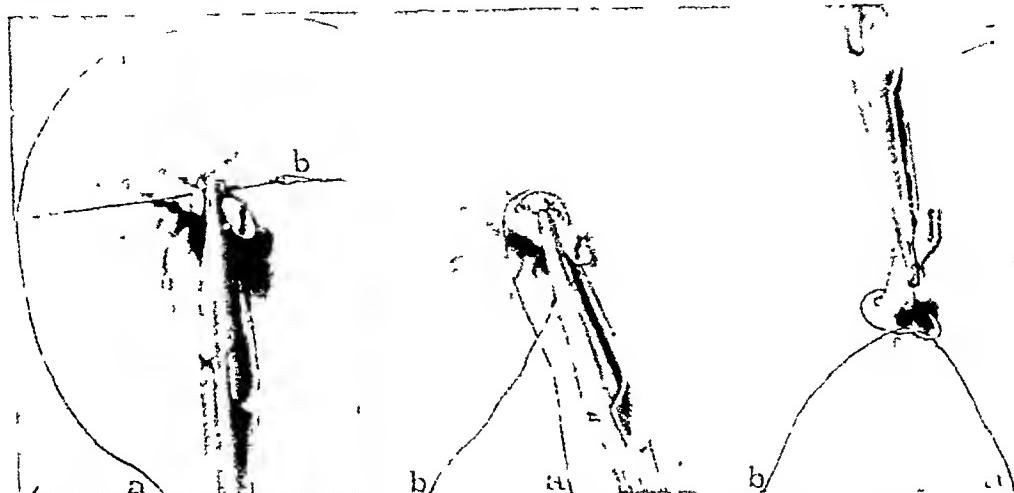


FIG. 3. The ligation of an isolated vein or artery by transfixion. The vessel has been twisted to prevent bleeding from the needle-prick. (From Halsted, William Steward. Ligatures and suture material. *J. A. M. A.*, 60: 1119-1126, 1913.)

Clean surgical cases should be dressed before infected cases. Stitches should be removed carefully, and care should be taken to avoid contamination when doing dressings.

*G. Special Postoperative Measures to Minimize Wound Infections.* Many postoperative measures are in use which are of vital importance to the patient. No attempt will be made to enumerate all of these measures; in fact, only those measures which are frequently neglected will be mentioned.

Postoperative pulmonary complications (many are due to emboli and a refined technic reduces their incidence) are often a direct or indirect factor in the development of wound infections. Every precaution should be taken to keep these postoperative complications at a minimum. Complete examinations should be made prior to the operation to make certain that no respiratory infection is present in cases scheduled for elective operations. Should respiratory infections be present in cases requiring emergency operations, determine their nature and take prompt postoperative measures for their correction.

While either helium-oxygen (helium 80 per cent; oxygen 20 per cent) or carbon dioxide in oxygen, (carbon dioxide 5 per cent) should be used for aeration of the lungs, neither should be depended upon alone. Of more importance is the frequent *deep breathing* (at least six deep breaths every half hour when awake) throughout the first three days of the postoperative period. Frequent deep breathing will be even more beneficial after spinal anesthesia than it will after general anesthesia, as the patient will be able to co-operate immediately after the operation. It is essential that patients be reminded frequently of the importance of deep breathing, otherwise they will neglect it, as deep breathing often increases their discomfort. The frequent change of position after operation should go hand-in-hand with deep breathing.

Atelectasis should be treated promptly by aeration of the lungs with carbon dioxide-oxygen and by placing the patient on the uninvolved side for certain periods. When the symptoms become distressing, with cyanosis and dyspnea, an oxygen tent should be employed. Many consider the bronchoscopic aspiration of the mucous

exudate as the treatment of choice, and it is especially recommended for extensive atelectasis or whenever symptoms are

blood volume and a blood transfusion given as soon as it is available to replace the loss of cellular elements of the blood.

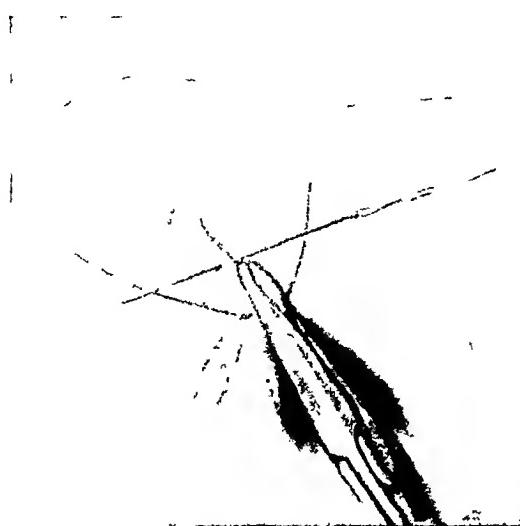


FIG. 4. The usual method of controlling hemorrhage from one or more vessels by transfixion. (From Halsted, William Steward. Ligature and suture material. *J. A. M. A.*, 60: 1119-1126, 1913.)

persisting after the above measures have been instituted. When respiratory infections occur after operations, they should be treated promptly, one of the sulfonamide group of drugs, particularly sulfathiazole, often being indicated.

Any condition which prolongs the convalescence or lowers the patient's resistance, may be a factor in the development of wound infections or complications. Therefore, it is essential that all measures be taken to avoid or minimize the occurrence of those conditions. Prostigmine is useful in preventing or decreasing distention, and it is usually given as a routine measure, unless contraindicated.

In prolonged illnesses or when duodenal suction has to be continued over a considerable period, a proper fluid balance should be maintained, with adequate electrolytes and vitamins. Blood transfusions are often necessary, or the administration of plasma may be indicated in order to obtain an adequate serum protein level. In the event of pronounced hemorrhage, plasma should be given at once to restore



FIG. 5. Ligation by transfixion of nonisolated vein, to be divided at  $\lambda$ . The clamp is on the tumor side of the vessel. (From Halsted, William Steward. Ligatures and suture material. *J. A. M. A.*, 60: 1119-1126, 1913.)

Wound repair is retarded by either a deficiency of proteins or a deficiency of vitamin C; therefore, a deficiency of either may be a definite factor in the development of wound disruption or postoperative hernia. Wound repair is also retarded by a high fat diet.

#### CAREFUL HEMOSTASIS AND GENTLENESS

When there has been proper preliminary investigation and adequate preoperative preparation, excepting a gross break in technic, then *careful hemostasis* is considered the most important factor in avoiding postoperative complications. It is even more important than gentleness. The importance of both careful hemostasis and gentleness can not be stressed too much, and they should go hand-in-hand in a refined technic.

#### PROPER SUTURE MATERIAL

*Silk.* In regard to the proper ligature-suture material, I would list fine black

twisted silk as best suited for clean surgical cases. Fine black twisted silk prepared according to the instructions given under

long. The silk strands are then dipped in melted bone-wax. The excess wax is wiped off and the silk is autoclaved.

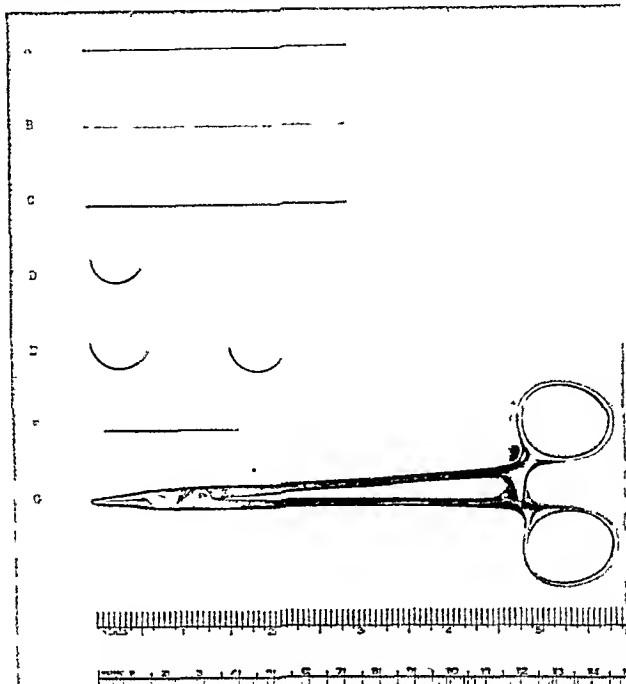


FIG. 6. A, No. 4 black twisted silk; B, No. 000 chromic catgut; C, No. 2 chromic catgut; D, No. 3 French needle; E, No. 3 Kelly intestinal needle and No. 12 Ferguson needle; F, milliner needle; G, small needle holder used in the silk technic.

"Silk Technic" is economical. Serum-proof silk has no advantage over twisted silk which has been waxed, and it is much more expensive. Silk can be used for interrupted sutures in slightly infected or in potentially infected cases, if extreme care is taken to avoid contamination; but in these cases it is advisable to use catgut sutures adjacent to the drain, whenever drainage is necessary. The use of silk in these cases should never be attempted by anyone who is not entirely familiar with all the details of the silk technic. Silk should not be used where gross contamination is unavoidable.

#### PRINCIPLES OF THE SILK TECHNIC

The following are some of the principles of the silk technic: No. 4 black twisted silk is ordinarily used for all purposes. The silk is wound around a board of sufficient length, so that the silk strands when cut across once will be approximately 18 inches

Another method of preparing the silk is to wind it around a board long enough so that the silk strands will be the desired length when cut across once; however, the silk is not cut until the time of the operation. The silk is waxed on the board and autoclaved. Small rubber tubing split in half is attached to the ends and across the sides of the boards. Shambaugh recommends adding an equal amount of vaseline to the beeswax. Starting the knot made with twisted silk which has been treated with only beeswax has a tendency to become untied. This danger is diminished when vaseline has been added to the beeswax. Shambaugh's experimental findings have been my clinical impressions since adding vaseline to the bone-wax.

Silk should not be sterilized several times as it loses its strength from repeated sterilizations. A small half-circle No. 2 or 3 French needle is used, except in gastro-

intestinal work in which a straight intestinal needle (milliner) is usually preferable. There are occasions when a No. 3 or 4 half-circle Kelly intestinal needle or a number 12 half-circle Ferguson needle may be substituted for the French needle, particularly when sewing through thick, dense fibrous tissue. It is best not to use the same silk suture more than once in a French needle as it may become frayed; however, this fraying could be avoided to a great extent if one were careful always to thread the French needle near the end of the silk strand, and never to pull the silk through the needle. A small needle holder must be used with French needles. The hemostats used for clamping the vessels must be small. One should attempt to clamp only the vessels; if any tissue is included in the clamp, it must be the smallest amount possible. There must be minimal tissue injury with careful sharp dissection. Gentleness must be observed and the maintenance of maximum blood supply should be the aim throughout the operation.

The strangulation of large amounts of tissue must be avoided, but all bleeding must be controlled immediately. Transfixion of ligatures should be frequently employed. The silk suture, the finest that will furnish the necessary strength, must be cut at the knot. The surgeon's knot is most satisfactory for silk; but where there is much tension or when ligating moderately large or large vessels, another throw (tied square) on the surgeon's knot will be necessary. When using silk, the single square knot may not be adequate for holding, especially if there is any particular tension. The weakest part of the suture is at the knot. The skin, subcutaneous tissues, muscles and fascia should be covered at all times until they are ready to be closed; when the peritoneum is opened it is attached to the laparotomy pads used to cover the edges of the wound. Silk sutures should be interrupted, except in the peritoneum where they may be continuous. However, continuous sutures must never be used in infected or in potentially in-

fected cases. When closing the peritoneum the sutures should be placed so the edges of the peritoneum will extend upward into the wound, in order that there will be no raw surface extending within the abdomen. The careful closure of all layers is most important, but no layer is probably as important as the peritoneum and transversalis fascia. The subcutaneous fat should be closed with interrupted silk sutures in order to close the dead space. A subcutaneous suture is used for the purpose of almost approximating the skin edges, and they should be placed so the knot will be underneath. The bite should be taken a short distance from the edge of the wound and should include only the deeper layers of the skin. These subcutaneous sutures are important; they help to keep tension off the skin sutures and aid in producing narrower scars. The interrupted skin stitch is considered the most suitable of all skin stitches. No suture should be placed under tension if it is possible to avoid it. Skin sutures should be just tight enough to approximate the skin edges. In order to avoid trauma, incisions should be of sufficient length to give adequate exposure. Care should be taken in removing sutures and in changing dressings. Silver foil is used to cover the incision; it helps to prevent contamination and infection.

#### COTTON

I have had only a limited experience with cotton as a ligature-suture material, but from this experience and from the literature, it would appear to be comparable to silk. It seems probable that cotton as a ligature-suture material will find a more general use in surgery as soon as its qualities become better known. Cotton is economical and so far the reports on its use as a ligature-suture material have been extremely favorable. Neither silk nor cotton should be used as a suture material except by those who have been trained in the silk technic or unless they fully understand and will carry out the rigid rules employed in the silk technic. In other

words, neither silk nor cotton should be employed in a manner similar to that employed when using large catgut; otherwise difficulties will surely be encountered. Certainly there should be no place in surgery for large sizes of nonabsorbable sutures, particularly using large nonabsorbable sutures throughout an operation.

#### FINE CHROMIC CATGUT

This clinical investigation of fine chromic catgut and the various articles appearing in the literature seem definitely to indicate its superiority to large catgut (chromic and plain). When it is considered that fine chromic catgut lasts longer in the tissues than the larger sizes, and any size of chromic catgut lasts much longer than plain catgut; and also taking into consideration the fact that plain catgut causes much greater reaction of the tissues—with delayed wound healing, then there is definite reason for using the smallest chromic catgut suture that has sufficient tensile strength for the period of healing. It is unusual for No. 0 chromic catgut (twenty day—medium) of the brand used in this investigation not to have adequate tensile strength. However, it may occasionally be necessary to use No. 1. The same results will not always be obtained with the same sizes of different brands of catgut because of the different methods employed in their manufacture. A suture may have adequate strength for the initial period of healing, but not enough strength for the entire period of healing. When using fine chromic catgut the sutures should be placed closer together than when using large sizes. The area of induration along the incision where fine chromic catgut has been used is less than it is when large catgut has been employed.

There was only one patient in the group of fine chromic catgut cases, in which the tensile strength of No. 0 chromic catgut (twenty day—medium) was not adequate for the entire period of healing. This patient had a cholecystectomy performed in

1935, and in 1936 he developed a ventral hernia in the region of the operative scar. In 1937, the hernia was repaired but it recurred in 1939. Examination of this patient revealed a moderately large ventral hernia along the upper right rectus in the region of the operative scar. The hernia was repaired, using No. 0 chromic catgut (twenty day—medium) as interrupted mattress sutures in the peritoneum and fascia, with the fascia being overlapped. The wound became infected, with the first sign of the infection becoming noticeable on the tenth postoperative day. The infection was not severe, as the drainage did not total more than a tablespoonful. The hernia recurred a few weeks after he got out of bed. This patient's poor health and his lack of care for himself after being allowed out of bed, are additional factors which probably had a definite bearing on the recurrence, although it is believed that the infection was the greatest factor. Several recurrent inguinal hernias are included in this group of fine chromic catgut cases, without any evidence thus far of recurrences.

When considering the reaction caused by plain catgut, the short duration it holds in the tissues, and also taking into consideration the fact that fine chromic catgut can serve better as ligature-suture material in any location than plain catgut, with the possible exception of ligating bleeders in the skin, there would appear to be an extremely limited field for the use of plain catgut in surgery. Fine chromic catgut as a subcutaneous suture should not be larger than size No. 0000, especially if the suture is near the skin. As long as physicians and hospitals continue to order the larger sizes of suture material—whether it be catgut or silk—the manufacturers will continue to produce them. It is the responsibility of the surgeon to see that he gets the correct suture material and that it is the proper size. There certainly will be less plain catgut used when the facts relating to its disadvantages, and those concerning the superiority of fine chromic catgut become better known.

## CORRECT USE OF PROPER SUTURE MATERIAL

In regard to the correct use of the proper suture material, it is recommended that the silk technic be employed when using silk, cotton or fine chromic catgut. Those who lack training in the silk technic should not use silk or cotton unless they use the smallest sizes, take extreme care to avoid contamination and follow the most rigid rules of technic. To those who lack training in the silk technic, it is recommended that they use fine chromic catgut. The finer the suture material used the more refined the technic becomes. For the average surgeon, fine chromic catgut appears to be the best suture material for general use at the present time.

## REPORT

I am well aware of the fact that definite conclusions can not be drawn from the number of patients in this series; however, the series is large enough to justify the forming of certain impressions. This series consists of unselected and consecutive cases in each of the three groups, and the primary purposes of this report are to compare the differences in infections, post-operative temperatures, etc., when using fine silk, fine chromic catgut and large catgut (chromic and plain).

In each of the three groups the following types of operations are included: appendectomy, herniorrhaphy, cholecystectomy, exploratory laparotomy and different gastro-intestinal procedures. The fine silk and large catgut groups included in addition, splenectomy, hysterectomy and various operative combinations upon the internal female organs.

More appendectomies and herniorrhaphies are included in the fine chromic catgut group, as a majority of the operations in this group were performed upon a younger age group of male patients. As the lowest temperatures are usually obtained in abdominal surgery when there has been either an appendectomy for chronic ap-

pendicitis or a herniorrhaphy for uncomplicated inguinal hernia, any difference existing between the three groups in regard to obtaining low postoperative temperatures would certainly be in favor of the fine chromic catgut group. However, many emergency operations are included in the fine chromic catgut group, particularly operations for acute appendicitis, some being perforated and several appendices being gangrenous; therefore, in regard to obtaining a clean wound, any difference existing between the three groups would be in favor of the fine silk and large catgut groups. The percentage of infections in operations for inguinal hernias is ordinarily rather high, but no infection occurred in either the fine silk or fine chromic catgut groups when operating for the repair of inguinal hernias.

*Fine Silk Group.* In some cases in the fine silk group, No. 1 chromic catgut was used to close the peritoneum; catgut was also used primarily in the pelvic part of operations upon the internal female organs, and in wounds adjacent to the drains. One brand of black twisted silk (champion) was used entirely in the fine silk group, No. 4 being used throughout, except for No. 7 which was occasionally used in suturing the fascia. The principles of the silk technic which have been described were observed in all cases in the silk group. Silver foil was used to cover the incisions in all cases in this group.

*Infections.* There were thirteen cases which were drained in the fine silk group, but there was no evidence of infection of the wound in any of these cases except immediately adjacent to the drain, and all of these drainage cases healed within a reasonable time.

There was only one infection in the clean cases in the entire fine silk group, and that occurred in a baby ten days old who had an infected umbilicus when he was operated upon. It is believed that the umbilicus was the source of the infection. There was no instance of either serum or hematoma in the fine silk group.

The late extrusion of silk knots occurred in three cases which had been drained (two cholecystectomies and one appendectomy). The wounds in all three cases had completely healed by the twentieth postoperative day. There was an extrusion of one silk knot in one case two months after the wound had healed, and an extrusion of two silk knots in the second and third cases about six weeks after the wounds had healed.

	Per Cent
Infections.....	0.9
Hematomas.....	0
Disturbances of primary healing .....	0.9
Wound disruption.....	0
Postoperative hernia.....	0
Extrusion of knots.....	2.4

*Postoperative Temperatures.* When using silk and following the principles of the silk technic, if the postoperative temperature goes above 100.5° F., one should look for complications. They will not always be present, but when employing silk and rigidly following the principles of the silk technic, postoperative temperatures are usually low, and a rise above 100.5° F. often indicates that something is wrong. The maximum postoperative temperature in the patient having the least elevation of temperature in the fine silk group was 98.8° F., and the operation was inguinal herniorrhaphy.

Clean surgical cases which usually run the highest postoperative temperatures are: hysterectomies (and various operations upon the internal female organs, particularly when there is infection present), cholecystectomies and operations upon the gastrointestinal tract. The hysterectomies and other operations upon the internal female organs with their tendency to develop infection of the urinary tract, and cholecystectomies were responsible for the majority of cases whose maximum postoperative temperatures were above 100.5° F.

	Per Cent
Maximum postoperative temperature less than 100° F.....	24
Maximum postoperative temperature 100° F. or less.....	35.2
Maximum postoperative temperature 100.5° F. or less.....	55.2

*Distention.* It is difficult or practically impossible to determine definitely the amount of postoperative distention. Any statement regarding the amount of distention would necessarily be an estimate; nevertheless, I believe that distention was considerably less in both the fine silk and fine chromic catgut groups than it was in the large catgut (chromic and plain) group. The use of prostigmine is believed to have been a definite factor in decreasing the distention in the fine chromic catgut group, as it was used routinely in about one hundred cases, but it could not have been a very deciding factor in the fine silk group as it was not used in more than twenty cases. Prostigmine, pitressin and duodenal suction were used only occasionally in the large catgut (chromic and plain) group.

#### FINE CHROMIC CATGUT GROUP

In the fine chromic catgut group, only one brand of catgut (Curity—medium—twenty day) was used and the sizes varied from No. 0000 to No. 0, except in ten cases No. 1 was used instead of No. 0. In this fine chromic catgut group, silk was used as a serosal suture in gastrointestinal anastomosis. When performing operations on the gastrointestinal tract, it is advisable to cover the area immediately surrounding the actual site of the operation with laparotomy pads moistened with an aqueous solution of zephran in order to minimize the possibility of contamination from intestinal contents. The pads are discarded as soon as the anastomosis is completed. A technic equivalent to the silk technic was employed in all cases in the fine chromic catgut group, except silver foil was not available for appendectomy incisions when drainage was not employed. While no figures can be given from this series on the

importance of silver foil in helping to prevent contamination and infection, I am of the opinion that it is a definite factor.

*Infections.* There were nine cases which were drained in the fine chromic catgut group, but there was no evidence of infection of the wound other than immediately adjacent to the drain, except in one case and then the slight infection extended only a short distance along the incision on each side of the drain.

There were six infections in the clean cases in the fine chromic catgut group, neither of which was serious, nor was hospitalization delayed more than a few days because of the infections. Four of the infections occurred in appendectomy wounds; one in a herniorrhaphy wound for recurrent ventral hernia (reported above) and another in a herniorrhaphy wound for incarcerated epigastric hernia, the peritoneum of the excised sac being inflamed clinically and verified by pathological report. This patient with the incarcerated epigastric hernia, had some inflammation of the skin and all underlying tissues including the peritoneum of the sac at the time of the operation. Since this was a case of infection it actually should not be included in a group of clean cases and would not, except for the fact the wound was not drained. There was one small hematoma in the fine chromic catgut group of cases, but the wound healed promptly without gross evidence of infection. The appearance of the infection in the appendectomy wounds occurred on the tenth day (postoperative) in two cases, and on the twelfth postoperative day in two cases. There was no case with serum that did not sooner or later show gross evidence of pus. The late extrusion of knots occurred in two cases; one knot in each case being extruded about six weeks after the wounds had healed.

	Per Cent
Infections	4.3
Hematomas	0.7
Disturbances of primary healing	0.5
Wound disruption	0
Postoperative hernia	0.7
Extrusion of knots ..	1.3

*Postoperative Temperatures.* When using fine chromic catgut and following the principles of the silk technic, if the postoperative temperature goes above 100.5°F., one should look for complications. A rise above 100.5°F. often indicates that something is wrong, as it does in the case of fine silk.

There was no case in the fine chromic catgut group in which the maximum postoperative temperature was less than 99°F., but there were three cases (two appendectomies and one inguinal herniorrhaphy) in which the maximum postoperative temperature did not exceed 99°F.

	Per Cent
Maximum postoperative temperatures less than 100°F	24.6
Maximum postoperative temperature 100°F. or less	36.6
Maximum postoperative temperatures 100.5°F. or less	60

*Distention.* In the fine chromic catgut group the number of cases with minimal distention closely paralleled those in the group in fine silk cases.

#### LARGE CATGUT (CHROMIC AND PLAIN) GROUP

In the large catgut (chromic and plain) group, the sizes varied from No. 00 to No. 2, the larger sizes being used most frequently, and different brands of catgut were used. There was not the refinement of technic which was employed in the fine silk and fine chromic catgut groups; in other words the technic employed was similar to that employed by the average surgeon using large catgut. Silver foil was not used on the incisions in this group.

*Infections.* In the large catgut group there were fourteen cases which were drained. In five of these drainage cases the incisions became infected; that is, there was evidence of infection of the wound in addition to the infection immediately adjacent to the drain. The remaining nine cases showed no infection except where the wound was drained. The fact that five out of fourteen drainage cases in this group showed considerable infection of the inci-

sion in addition to that adjacent to the drain, would seem to indicate that silver foil is of importance in keeping these incisions clean except where they are drained.

In the clean cases in the large catgut (chromic and plain) group there were infections of the wounds in sixteen instances: three cases of a small amount of serum which soon healed without gross evidence of pus, five cases of serous drainage which soon became purulent, and eight frankly purulent cases from the very beginning of the infection. One of the patients whose infection was purulent became extremely ill as a result and it was six weeks before the wound healed. There was a moderately severe infection which occurred unusually late, the first evidence of the infection appearing on the twenty-third postoperative day. The wound in this case drained four weeks. In addition there were five cases in this group which developed hematomas, three of which soon developed gross evidence of pus. There were three patients which developed postoperative hernias in this group. One postoperative hernia (or recurrent inguinal hernia) followed the repair of an inguinal hernia which developed a moderately severe infection of the wound; another postoperative hernia developed after an operation upon the internal female organs, in which drainage was necessary and the wound became infected in addition to that adjacent to the drain and the third postoperative hernia developed in a patient who had had two previous operations: one a low midline incision for salpingo-oophorectomy and appendectomy, and the other a long upper right rectus incision for cholecystectomy.

There was one patient who developed a disruption of the entire wound down to the fascia on the tenth postoperative day. This patient had had very slight drainage at the lower end of the incision (low midline) but it had practically ceased, and she was to be discharged from the hospital on the day the disruption occurred. The disruption occurred about two hours after the skin

stitches had been removed, and followed immediately after an attack of unexplained vomiting. There was a secondary closure of this wound one day after the disruption and the wound had healed by the thirtieth post-operative day. The remarkable thing about this disruption is the fact there was complete disruption down to the fascia, without any evidence then or later of the fascia, muscles or peritoneum being affected.

There were extrusions of knots in three cases after the wounds had apparently healed. The extrusion of the knots occurred from one to four weeks afterward.

	Per Cent
Infections.....	17.1
Severe infection (3 cases).....	2.7
Moderate infection (4 cases).....	3.6
Slight infection (9 cases).....	8.1
Serum (3 cases).....	2.7
Hematomas.....	1.6
Disturbances of primary healing.....	18.7
Wound disruption (incomplete).....	0.8
Postoperative hernia.....	2.4
Extrusion of knots.....	2.4

*Postoperative Temperatures.* In the large catgut (chromic and plain) group there was no case in which the maximum postoperative temperature did not exceed 99°F. It will be noted that there is a marked difference between the percentage of low postoperative temperatures in the fine silk and fine chromic catgut groups and the large catgut (chromic and plain) group. The lower the postoperative temperatures, the more comfortable the patients and the fewer the complications.

	Per Cent
Maximum postoperative temperature less than 100°F.....	9.6
Maximum postoperative temperature 100°F. or less.....	21.6
Maximum postoperative temperature 100.5°F. or less.....	34.4

*Distention.* Distention was considerably more marked and troublesome in the large catgut (chromic and plain) group. While the more frequent use of prostigmine and duodenal suction in the fine silk and particularly in the fine chromic catgut groups were definite factors in relieving or

decreasing distention, nevertheless, the impression has been gained that the distention was certainly less in these two groups than in the large catgut (chromic and plain) group, when neither of these measures was employed.

#### CONCLUSIONS

1. The more refined the surgical technic, the smoother will be the convalescence with fewer complications, regardless of the suture material employed.

2. Low postoperative temperatures throughout the convalescence usually mean low morbidity and low mortality rates.

3. Fine silk is slightly superior to fine chromic catgut in the following respects: (a) wound infections, (b) slightly less tissue reaction, and (c) fewer wound disruptions and postoperative hernias.

4. Fine chromic catgut is superior to fine silk in the following respects: (a) It is more suitable for infected cases and for general use, and (b) it is easier to employ.

5. Fine chromic catgut when employed according to the principles of the silk technic is superior to large catgut (chromic and plain) as ordinarily used in the following respects: (a) wound infections, (b) low postoperative temperatures, (c) wound disruption and postoperative hernia, (d) postoperative complications, (e) less tissue reaction, with more rapid healing of the wounds, and (f) greater holding strength over a longer period of time, when it is most needed.

6. Fine chromic catgut is preferable to plain catgut as a ligature-suture material in abdominal surgery, with the possible exception of ligating bleeders in the skin.

7. Large sizes of suture material should not be used throughout an operation.

8. When employed according to the principles of the silk technic, either fine silk or fine cotton appears to be the suture material of choice in clean surgical cases. However, for the average surgeon, fine chromic catgut appears to be the best

suture material for general use at the present time.

9. Incisions should be of sufficient length to give adequate exposure.

10. Deep breathing and frequent change of position, when properly carried out during the first few days of the postoperative period, are factors in preventing postoperative pulmonary complications, particularly atelectasis.

11. Hemorrhage, trauma and infection are important factors in producing postoperative discomfort and complications.

12. Careful hemostasis is one of the most important factors in avoiding postoperative complications.

13. To be able to operate quickly and at the same time to observe certain well defined principles of surgery, such as careful sharp dissection, careful hemostasis and gentleness is a highly skilled accomplishment, but the surgeon should never attempt to hurry through an operation in a good risk patient. For the extra time spent in employing a careful technic, the surgeon will be well repaid with lower morbidity and mortality rates.

I wish to express my appreciation to The Lewis Manufacturing Company for their generosity in furnishing an adequate supply of fine chromic catgut for this clinical investigation.

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# REIMPLANTATION OF THE TIBIAL SPINE IN AVULSION FRACTURE OF THE ANTERIOR CRUCIAL LIGAMENT\*

W. RUSSELL MACAUSLAND, M.D.

BOSTON, MASSACHUSETTS

**A**CCURATE reduction of fractures of the tibial spine due to avulsion of the anterior crucial ligament is

bed by the organized blood clot in the fracture cavity.

Avulsion fractures of the tibial spine



FIG. 1. Avulsion fracture of the entire spine of the tibia with displacement.

FIG. 2. Screw fixation of the fragment three days after the injury.

essential to the preservation of the stabilizing strength afforded by this ligament in the knee joint. That the fragment, when displaced to any appreciable extent, can be accurately replaced by the generally accepted method of treatment is to be questioned. Surgeons for the most part still advise conservative manipulation in fresh fractures, believing that upon extension of the knee, the fragment falls back into its tibial bed. However, not only is it difficult to obtain complete extension of the knee in the presence of the marked distention that accompanies such fractures, but the fragment, displaced and often rotated, cannot be controlled and forced into its bed by extending the joint. Even if extension and replacement were possible, the fragment would tend to be lifted from its

with displacement are best treated by operative reduction and fixation of the fragment. From time to time operators have attempted to point this out and to suggest methods of fixation. Suturing of the bony fragment in place has been advocated, and a particularly satisfactory method has been suggested by Lee. Another method, which would seem to have certain advantages over the suture procedures, is the fixation of the fragment by means of a screw. This method is a simple one and easily carried out. Through the operative exposure accurate replacement of the fragment is made possible, and by the screw fixation more secure retention of the fragment is insured than by the suture methods. Motion may be safely instituted at an earlier period than following fixation by

\* From the MacAusland Orthopedic Clinic, Boston.

sutures, which might give way under tension, and the convalescence is thereby shortened.

*Operative Technic of Screw Fixation.* The knee is prepared and flexed to a right angle. A tourniquet is applied to the upper thigh.

An incision is made through the skin and fascia, in the midline of the knee, beginning over the quadriceps tendon about three inches above the patella and running down over the patella to a point below the tibial tubercle. The quadriceps tendon and patellar ligament are split, and the periosteum over the patella is incised. The patella is sawed through vertically in the center, and its halves together with the divided quadriceps tendon and patellar ligament are retracted laterally.

The semilunar cartilages are inspected, and if damaged, are removed. The fracture cavity and the surface of the fractured tibial spine are carefully cleaned of blood clots and fibrous strands. The tibial spine is replaced in its bed, and a screw is placed through the attachment of the anterior crucial ligament and the midportion of the fragment and tightly set into the tibia.

The capsule of the joint is closed with fine chromic catgut. The quadriceps tendon, the patellar ligament and the fascia over the patella are sutured with inter-

rupted chronic catgut, and the skin is closed with silk sutures.

The knee is immobilized in a posterior plaster shell in the position of from 10 to 15 degrees of flexion. After ten days contraction of the quadriceps should be practised daily. At the end of three weeks the shell is removed, and the patient acting as his own guide may begin to move the knee gently. Hot fomentations are of benefit at this time.

#### CASE REPORT

M. S., a girl aged sixteen, injured her left knee in an automobile accident. The roentgenographic examination showed that the entire tibial spine had been avulsed by the anterior crucial ligament. The fragment was well elevated from its tibial bed. (Fig. 1.)

Operative fixation was carried out on the third day after the injury according to the technic that has been described. Damage to the subpatellar fat pad necessitated its removal. (Fig. 2.)

*End Result.* Four months after the operation, the knee is stable, painless and has a full range of motion. The patient is able to dance and to do everything she wishes.

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# Case Reports

## TUBERCULOSIS OF THE GREATER TROCHANTER\*

WALTER G. STUCK, M.D.

Chief of Orthopedic Surgery,  
Robert B. Green Hospital

AND

JOHN J. HINCHEY, M.D.

Resident in Orthopedic Surgery,  
Robert B. Green Hospital

SAN ANTONIO, TEXAS

AS is generally known, tuberculosis of the shaft of the long bones is relatively rare as it occurs in only 3 per cent of all cases of bone and joint tuberculosis. A quite unusual manifestation is tuberculosis of the upper end of the shaft and greater trochanter of the femur. Myerding and Mroz reported nineteen such cases in 1933 and listed a complete bibliography. In the case we have recently observed there was extensive involvement of the upper end of the shaft of the femur although there was no infection of the hip joint.

Beneath the gluteus maximus muscle there is a large bursa over the lateral aspect of the greater trochanter which seems to be a favorite site for the development of the tuberculous infection. It is from this bursa that the infection may spread until the bone becomes extensively involved. In the cancellous bone of the trochanter spread of the infection takes place easily until there is much destruction of bone. Involvement of the bursa alone is more common in children, while accompanying infection in the bone of the trochanter occurs mainly in adults. Swelling about the trochanter of many months' duration, local nonfebrile fluctuating masses, aching pain, and limp are the most typical signs and symptoms. X-rays reveal erosion of bone and occasional sequestra although there may be no bone changes in those cases in which only the bursa is involved.

The most satisfactory treatment of

tuberculosis of the greater trochanter is complete excision of the infected tissue and closure of the skin without drainage in order to forestall the dangerous secondary infection or troublesome chronic sinus formation. In our present case it was not deemed wise to close the wound because of the extensiveness of the infection in the bone. Nevertheless, the use of powdered sulfanilamide in the wound prevented the development of secondary infection and the wound healed promptly after the pack was removed.

### CASE REPORT

A. O., a fifty-two year old Mexican man was first observed September 8, 1941, because of burning pain in his right hip which he had noticed for eight months. At the onset a hard red spot, the size of a quarter, had appeared in the region of the right greater trochanter. He applied a salve and an abscess formed which had drained off and on ever since.

The patient worked as a ranch hand in Mexico until he was thirty years of age and was a coal miner several years subsequently. In 1922, he was caught in a cave-in of a mine and received a simple fracture of the lower end of the right femur and a simple fracture of the upper end of the right tibia. Four months after this accident a small piece of bone worked out at the medial side of his right knee and was removed. There had been no subsequent drainage, pain or stiffness of the knee. His right leg has been three-fourths inch shorter than the left ever since the accident which had caused a slight limp.

\* From the Orthopedic Service of the Robert B. Green (City-County) Memorial Hospital, San Antonio, Texas.



FIG. 1. X-ray of hip before operation showing extensive involvement of the greater trochanter with calcified masses about the upper end of the femur.



FIG. 2. X-ray of hip after operation revealing removal of all infected bone and most of the calcified areas.

The patient has been married twenty-four years and has had one stillborn child. There was no history of tuberculosis, lues, or other familial disease.

Examination revealed a Mexican adult male of average size who walked with a scarcely noticeable limp. An open sinus about  $\frac{1}{8}$  inch in diameter was present on the lateral side of the right thigh directly over the greater trochanter. The skin around it was indurated for about an inch in all directions. Six inches distal to the sinus was an indurated reddened area the size of a quarter which had been present two weeks. There was no limitation of motion of the hip joint nor was any tenderness elicited on manipulation or deep pressure over the hip. The right leg was  $\frac{3}{4}$  inch shorter than the left.

Urinalysis was negative. There were 3,840,000 red blood cells with 10.5 Gm. hemoglobin, 5,650 white blood cells with 66 polymorphonucleus and 32 lymphocytes. Kline and Kahn tests were negative.

Smears and cultures from the draining sinus over the trochanter revealed the presence of *Staphylococcus aureus*.

X-ray revealed an old fracture at the junction of middle and lower third of right femur. There was destruction of the upper end of the femur with loss of the entire greater trochanter and the top of the neck of the femur. There were numerous large, round, calcified masses in the soft tissue surrounding the upper end of the femur. (Fig. 1.) X-rays of the chest were negative for evidence of tuberculosis.

On September 20, 1941, under spinal anesthesia a lateral incision was made over the right hip, the gluteus medius and the tensor fascia femoris muscles were separated and the neck of the femur and greater trochanter

exposed. Several small pieces of dense, calcified tissue were found completely separated from the shaft and neck. These were removed as were calcified masses in the greater trochanter and upper end of the shaft of the femur. After all necrotic tissue was removed, powdered sulfanilamide was sprinkled in the wound and it was packed with vaseline gauze. (Fig. 2.) Skin edges were brought together loosely. The gauze pack was removed at the end of three weeks and the wound healed promptly in the next three weeks.

Pathological examination of tissues removed revealed giant cells arranged in tubercle formation and degenerated areas which were undergoing calcification.

#### COMMENT

This patient was older than most of those who contract tuberculosis of the greater trochanter and his symptoms were of unusually short duration. From the history and the x-rays we suspected the presence of coccidioidal granuloma although pathological examination later proved the lesion to be tuberculous. The use of powdered sulfanilamide in the wound was undoubtedly of great value in the prevention of chronic sinus formation.

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# OSTEOGENIC SARCOMA AS THE CONCOMITANT OF AN INDUSTRIAL ACCIDENT\*

RODNEY F. ATSATT, M.D.

Chief of Orthopedic Division, Santa Barbara Clinic

SANTA BARBARA, CALIFORNIA

THE rather dry subject of bone tumors is best introduced by an interesting case history:

The patient, a genuine western cowboy with all the palaver and songs of a true Texan puncher, was twenty-nine years of age. He was born in Mucculla County, Texas. He began riding horses at the age of three years and had ridden them good and bad with the best of them. His right kidney had been jarred loose and there were many scars of accidents scattered over his body.

One of these accidents happened on April 12, 1939. At that time he was employed as cow hand by Ladder Ranch, Hillsboro, New Mexico. He was riding on the rim of a mountain when his horse stepped on ledge rock, tried to leap, his forefeet slipped and the horse and patient fell over backward. The patient rolled down the mountain side to lodge in oak brush with his right leg lying on a ledge of rock and with the fibular side down against the hard surface. The horse came down and rolled over the leg while in that position. The cowboy reported the accident to the foreman and general manager and was away from work three days. His leg did not bother him until March, 1940. X-rays were taken at that time and "a white cloud" was seen, surrounding the small bone. Gradually the leg became more painful and it grew in size. He returned to Texas in 1940, and on July 20, a four-inch section of the fibula was removed. Following this operation he was not uncomfortable until about November 1 when the leg began to ache constantly with occasional periods of sharp, boring pain. The pain and ache were worse at night. About December 10 the patient's leg was x-rayed in Prescott, Arizona, and it was found that the tumor had returned. Amputation was suggested by the attending surgeon. The patient notified his present employer who brought him to Santa Barbara from the ranch in Arizona.

On December 31, 1940, a midthigh amputation was done, turning a long anterior flap. The wound healed slowly. Inguinal nodes were subjected to a short course of x-ray therapy.

The roentgenograms previous to the amputation are depicted in Figure 1. X-rays of the chest were negative for metastatic tumor.

The pathological report is as follows: "The specimen is the right leg and distal third of the thigh. There is a well-healed scar 15 cm. in length on the lateral side of the lower leg. (Fig. 2.) Underneath the scar is a large, firm mass which on dissection is found to be intimately connected with the fibula, and the entire tumor and fibula are removed in one piece. (Fig. 3.) The tumor is oblong in shape, is infiltrating the muscles, especially the peronei. It is whitish in color, quite hard, and sections with difficulty. The internal appearance of the tumor is whitish-yellow. The consistency varies from very hard to very soft as one approaches the center."

The microscopic examination revealed the following: "Sections of tissue show the characteristic picture of osteogenic sarcoma. (Fig. 4.) The tissue is extremely cellular. The cells are large, though varying greatly in size and shape. The nuclei are prominent and many possess two or more nucleoli. Between the cells there is a hyaline, ground substance which in areas has the contour of bone spicules and in some areas shows remaining calcium deposits. The bone structure is of cancellous type without the presence of laminated markings or haversian canals. In areas there are scattered hemorrhages which have occurred from thin-walled vascular sinuses. Some of these sinuses show penetration by the tumor cells. (Fig. 5.) Innumerable atypical and unbalanced, bizarre mitotic figures are encountered. The picture is characteristic of an osteogenic sarcoma with a high degree of malignancy." (Wray Tomlinson, Pathologist.)

\* Read before the Western Academy of Orthopedic Surgeons, November 14, 1941.

With this case history as an introduction we wish to review briefly the general subject of bone tumors.

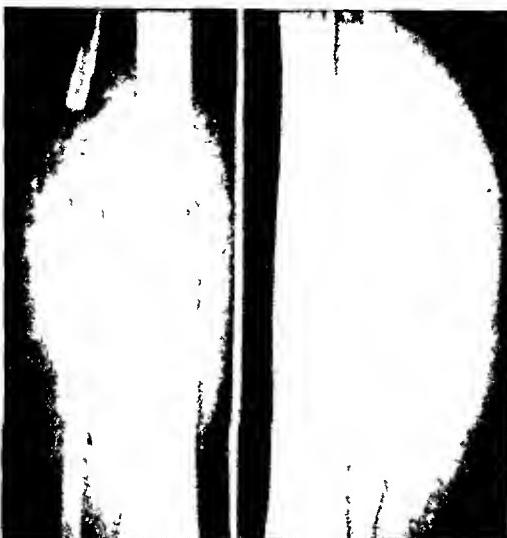


FIG. 1. Anteroposterior and lateral roentgenograms of tibia and fibula revealing operative defect in fibula and cloudy tumor mass.

The benign are of two general classes: (1) *osteomas* arising from the surface of long bones usually in the end zones, which may be compact or cancellous. These are usually multiple, frequently hereditary or traumatic and during their period of growth are often capped by a disc of cartilage. (2) *Chondromas* are cartilagenous tumors which occur ordinarily before the age of twenty and are located in the long bones of hands and feet. They are usually lobulated, encapsulated and may be cystic. It is believed that occasionally they may show sarcomatous changes.

The malignant tumors of bone are of four general classes: (1) *Osteogenic sarcoma*, (2) *Ewing's tumor*, (3) *myeloma* and (4) *giant cell tumor* (on occasion).

This discussion is restricted to the first class of the malignant tumors.

The term, *osteogenic sarcoma*, implies that it arises from cells whose function it is to form bone. The tumors are commonest in the second decade. They occur most frequently in the shafts of long bones and in the region of the knee joint.

*Symptoms and Signs.* Approximately five months go by in the average case before

the aching pain sends the patient to the doctor. He then often recalls some type of trauma connected with the location of the pain. This aching discomfort rapidly becomes severe and constant and disability results. Since most of these lesions are in the neighborhood of the knee joint, stiffness, a limp, and crutches follow, but even with complete rest the pain does not disappear. Accompanying these symptoms are leucocytosis, lymphadenitis and fever with secondary anemia. This enlargement of the regional glands often occurs irrespective of the fact that transmission is via the blood stream.

*Examination.* Physical examination reveals a large mass near the flexed knee joint, rubbery in consistency. This feels larger than the x-rays indicate, but is only slightly tender to touch.

*Roentgenology.* Early x-rays show merely a translucent zone about the bone with some raising of the adjacent periosteum. Later x-rays show combined central and periosteal involvement with small marginal lip. The old shaft is visible but is permeated by the tumor, indicating the tumor's invasive character. As the result of the osteolytic and osteolastic activity, the sun ray appearance is often produced. This characteristic activity is reflected also in the widespread invasion into the soft tissues.

*Gross Pathology.* The tumor may impinge the medulla, shaft and periosteum, creating a fusiform swelling. On section the ray formation may be evident and the tumor is seen as having a variety of textures depending upon what elements of bone and bone-forming substances are involved. There may be pearly grey areas of cartilage with cysts and hemorrhage, dense stroma with closely packed tumor cells, bone spicules and masses of bone. As has been said, the gross appearance depends on the relative amount of the different bone or bone-forming substances.

*Microscopic Pathology.* As indicated in the description of gross pathology the microscopic detail of the tumor varies with



FIG. 2. Well healed operative scar on bulging lateral aspect of leg.

FIG. 3. Tumor split *in situ*.

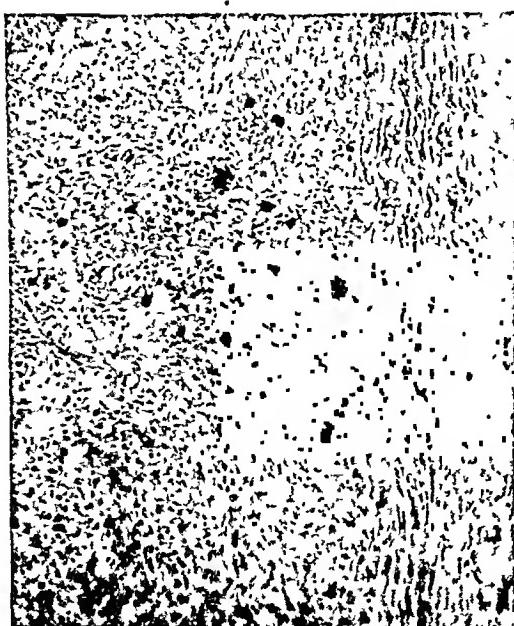


FIG. 4. Tumor (low power) invading muscle tissue.



FIG. 5. High power of tumor tissue.

its composition and covers the whole field of embryology of bone.

There are two main types of tissue: the cells and the stroma. Examining the cells there may be seen at first sight the pleomorphic osteoblasts for they dominate the picture with their hyperchromatic nucleii and mitotic figures. In another area in the same section the irregular cartilage cells may be prominent. Again the spindle-shaped tumor cells may fill the field, or here and there may be a few giant cells. Occasionally, osteoclasts are seen at work tearing down old bone trabeculae.

Turning our attention to the stroma or supportive framework, we may find hyaline or fibrocartilage, myxomatous, osteoid or finally osseous tissue. Every stage of bone growth may be represented in an osteogenic sarcoma, or one type may predominate.

*Classification.* Ewing's method of classification is based on the origin of the tumor, i.e., (1) periosteal, (2) medullary and subperiosteal, (3) sclerosing and (4) telangiectatic.

#### DISCUSSION

This stoical cowpuncher waited longer than normal after his accident before consulting a doctor. Instead of the average five months, eleven months had elapsed between the accident and the first consultation. X-rays at that time showed a "cloud" around the bone which was interpreted as callus about a healing fracture. It was not until the tumor reached sizeable proportions that it was taken seriously. Five months after the x-ray discovery of the tumor, a four-inch section of the fibula was removed. Six months later the tumor was again very large and painful and amputation was done at the midthigh level.

The record of events seems to start very definitely at the time when the patient's

leg was crushed, fibular side down, against the rock. In the patient's mind at least there is a definite causal relationship therein. However, we can not say with certainty that this industrial injury was definitely the cause of the disability\* but the sequence of events is so striking as to invoke the old rule of evidence, "Res ipsa loquitur."

#### SUMMARY

The patient, a western cowboy, was injured in an accident, while riding the range in April, 1939, in which his horse rolled over his leg lying fibular side down on a piece of rock.

In March, 1940, he began to have pain in the leg and an x-ray showed a "white cloud" surrounding the small bone which was interpreted as callus following a fracture.

In July, 1940, a four-inch section of the fibula was removed. In November, 1940, the leg began to be painful and in December an x-ray revealed the return of the tumor and the patient was brought to Santa Barbara. On December 31, a mid-thigh amputation was done.

Microscopically, the tumor was a large firm mass, oblong in shape and infiltrating the muscles. It was whitish in color and quite hard although the consistency in the central areas was very soft. The tissue showed the characteristics of osteogenic sarcoma. This tumor arises from cells whose function it is to form bone and, thus, is made up of all the elements of bone formation. In the usual case approximately five months pass between the time of injury and the time when aching pain sends the patient to the doctor.

\* This tumor is registered as Accession 72666, Army Medical Museum.



# TREATMENT OF DELAYED TONSILLECTOMY HEMORRHAGE

R. L. GORRELL, M.D.

CLARION, IOWA

THE practitioner who is confronted with late bleeding following tonsillectomy often wishes that the authorities who write so briefly and nonchalantly were at hand. The necrotic tissue cannot be grasped in the usual manner with a hemostat; sutures tend to cut through; local applications are of temporary effectiveness only; injections of the various sera are ineffective. Bleeding usually occurs in patients with infected tissue, so that the more manipulation is carried out, the more chance there is of spreading infection both locally and in the blood stream.

## CASE REPORTS

CASE I. John R., age ten, had had a tonsillectomy some ten days previously by another physician. No complications at the time or later was noted. On the ninth postoperative day, bleeding suddenly appeared and without obvious cause. It ceased spontaneously only to reappear in a few hours.

This process was repeated several times, before help could reach them through the heavy snows. When the youngster was lifted up into the car, blood poured from his mouth in a stream and he became syncopie. A sponge holder containing a large square of gauze was forced up into the tonsillar fossa and held there until the hospital was reached.

The hemorrhage had stopped by the time the boy was carried into the hospital. No local treatment was carried out, because the boy was in shock. A citrated transfusion was begun at once and 500 cc. were given.

He did not bleed one drop following the transfusion and was dismissed in twenty-four hours in good condition. No definite bleeding point was seen in the throat; no blood dyscrasia was discovered at the time, or since, and he has remained in good health since 1937.

CASE II. Mrs. A., age twenty-nine, suffered a streptococcic pharyngitis, followed by otitis

media. Her tonsils remained persistently infected and I removed them one month later. The left tonsil, on the same side as the affected ear, was spongy, contained much purulent material and tended to ooze a drop occasionally afterward. She went home the next morning, however, with a dry throat. She was given calcium gluconate and lactate powder, vitamin K and bile salts.

On the second postoperative day, she came to the office because of slight oozing from the left tonsillar fossa. The right fossa was clean; the left was markedly reddened and edematous and there was a little bleeding from the posterior surface of the anterior pillar which stopped when a solution of ferrie chloride, glycerin and tincture iodine, equal parts, was applied.

On the third postoperative night, she awoke with steady bleeding from the fossa. Powdered cocaine was applied and nupercaine solution for local anesthesia. Procaine solution could not be injected because the soggy tissue bled on being touched with the needle. Suturing and clamping were ineffective; compression with gauze soaked in adrenalin and bismuth subgallate checked the bleeding temporarily.

Five hundred cc. of the husband's blood was given to her by the citrate method. Within twenty minutes, the bleeding, which had been steady for four hours, stopped and did not recur.

She left the hospital in twenty-four hours and has been in perfect health since that time. It might be of interest to mention that complete blood studies both before and after operation disclosed nothing abnormal; urinalysis was negative.

CASE III. Mrs. H., age forty-seven, was operated upon by another physician in 1936. She had a fever of 100°F. the next day (a not unusual occurrence) but was dismissed in apparent good condition.

Six days later, she returned because of swelling of the side of the neck and soreness in the tonsillar region on that side. No bleeding occurred at this time. The lateral aspect of the

neck was obviously enlarged and moderate tenderness was noted over the rounded swelling. The tonsillar fossa was moderately swollen but contained only the usual membrane. Under rest in bed, hot packs and analgesics, the pain decreased and the swelling diminished in size during the next three days. She was dismissed, feeling fairly well.

On her return, two weeks following the tonsillectomy, the swelling was larger than ever, she was having marked pain in the area and a fever of 102°F. was present. The swelling was definitely indurated at this time, and the attending surgeon made a diagnosis of post-tonsillectomy cervical abscess. While the instruments were being sterilized, the surgeon went off to see other patients.

Sudden spontaneous hemorrhage occurred from the tonsillar fossa, which did not at first appear serious and the surgeon applied gauze packs and local applications which slowed down the bleeding. The structures were so edematous and indurated that suturing and clamping were not feasible. The carotid artery could not be ligated because of the indurated mass, the size of a large grapefruit, overlying it. The patient went into shock and died before a transfusion could be given.

#### DISCUSSION

To any one who has seen bleeding patients stop bleeding and recover quickly after a transfusion, it seems obvious that replacement of blood volume and proteins by a transfusion is the simplest and best treatment. It is unfortunate that the classification of tonsillectomy into an otolaryngologic procedure tended to separate it from other surgical undertakings and into the hands of men who had little or no experience in the technic of or benefits to be derived from transfusion. Now that serum transfusions can be given so easily, there will no doubt be an increase in the number of transfusions given.

A review of the literature available shows what procedures are recommended by various authors:

Christopher<sup>1</sup> advises rest, ice collar, morphine, astringents (ferric chloride, compound alum powder) or coagulants as thromboplastin or fibrogen, direct pressure

with gauze or forceps, ligation of bleeding point, and ligation of carotid artery.

Bailey<sup>2</sup> recommends packing into the wound a strip of gauze, which may be moistened with viper venom solution, turpentine or 50 per cent dextrose solution, making sure that it is packed *snugly* into the fossa; it is removed in fifteen minutes and the pulse counted every one-half hour to give warning of recurrence. If ineffective, ether anesthesia should be administered and the cavity packed again with moist gauze. This should be allowed to remain for five minutes. Then ligation should be done, if the bleeding point is found, or a small gauze swab should be placed in the cavity and the pillars sutured over it, taking care to pick up the muscle with each stitch. If bleeding is severe, a transfusion should be given (why wait until it is severe?) and the bleeding stopped by packing or by pressure of gauze squares held in sponge holding forceps against the ascending ramus of the jaw. Ligation of the external carotid artery should follow and the surgeon should make sure that the ascending pharyngeal branch, which comes off near the origin and on the inner surface has been included. Rarely does the opposite external carotid artery require ligation, as it affords the only free anastomosis.

Lederer<sup>3</sup> states that before operating the surgeon should inspect the pharynx for anomalous arteries and palpate the region of the tonsil to detect any unusual pulsation. He should apply pressure with a gauze sponge held over the bleeding tissues; apply adrenalin or saturated solution of tannic and gallic acid; clamp the bleeding point and follow this by suture-ligature. In case of severe hemorrhage apply digital pressure on the carotid artery at the point where it is felt pulsating just below the larynx (sixth cervical vertebra). Pressure should control hemorrhage sufficiently long to permit ligation of the external carotid artery. Blood should be given intramuscularly or by transfusion.

Hall<sup>4</sup> suggests the removal of the clot, which procedure often stops hemorrhage;

the application of pressure on the fossa with cotton or gauze balls moistened with hydrogen peroxide; suture-ligation of bleed-

stops oozing, and clamps or clamps and sutures.

Coolidge<sup>8</sup> applies direct pressure with

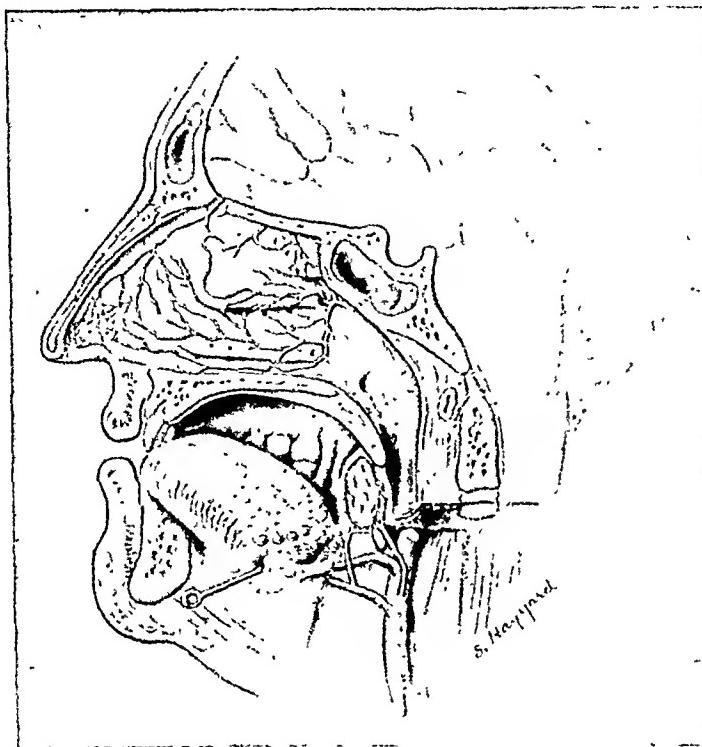


FIG. 1. The blood supply of the tonsil.\*

ing point; clamp-forceps which press on fossa and behind the angle of the jaw. "In late hemorrhage, there is a bleeding point in the middle of a bed of granulation tissue which is practically impossible to catch with forceps. Pressure is the best method; deep under-stitching can be tried."

Coakley<sup>5</sup> states that each bleeding point should be ligated with fine silk at the time of operation; recurring hemorrhage is treated by gauze pressure and ligation.

Turner<sup>6</sup> recommends hydrogen peroxide sponges; clamping and ligature of bleeding vessel; the application of pressure by means of a sponge in a sponge-holder, which is held firmly in the bleeding fossa, directed from the opposite angle of the mouth.

Morrison<sup>7</sup> applies pressure with a gauze sponge moistened with adrenalin, injects local anesthesia, the edema of which often

gauze sponge. Three deep sutures are passed from behind forward, through the posterior pillar, constrictor muscle and anterior pillar, and tied, thus obliterating the space made by removal of the tonsil.

Thorek<sup>8</sup> recommends that the surgeon look for marked pulsation, which indicates the close proximity of a large vessel, before operating, and that he know the anatomy of the external carotid artery, as ligation of the internal or common carotid arteries usually fail.

#### CONCLUSIONS

1. In case of persistent or marked bleeding, it is safest and most effective to give a blood transfusion. One fatal case is reported in which this precaution was not taken.

2. It is dangerous to stop bleeding at the time of operation with adrenalin applied locally, as the hemostasis may be only temporary.

\* Parke-Davis and Company kindly granted permission for the use of the cut from "Therapeutic Notes."

3. Hemorrhage is often stopped by a blood transfusion.
4. Hydrogen peroxide applied locally or by gargling will often stop oozing of blood.

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ENLARGED nodes in the postauricular and occipital areas and in the posterior triangle are, notably in children, strongly suggestive of pediculosis capitis, and call for a search for pediculi or "nits."

# THE TREATMENT OF HEPATIC CIRRHOSIS BY THE COMBINED USE OF THE TALMA OPERATION AND INSULIN

## CASE REPORT

J. M. BODENHEIMER, M.D.

Visiting Surgeon, T. E. Schumpert Memorial Sanitarium  
SHREVEPORT, LOUISIANA

A CAREFUL search of the records of the Shreveport Charity Hospital from 1924 to 1940 fails to show a single case of cirrhosis of the liver discharged cured. More than 90 per cent of the patients died in the hospital, while the remaining 10 per cent were probably sent home to die. Bettman in Forsheimer's "System of Medicine" is certain that a well established cirrhosis of the liver cannot be cured anatomically. As for ascites, it is a grave symptom. "Its occurrence," according to Rolleston, "has always spelled the doom of the patient." The literature up to 1928 gave two to five months as the average life after ascites appeared. Today writers are more liberal and concede a span up to two years, granted the patient has been under proper care.

While there have been reports of spontaneous cures of ascites, nevertheless the rarity of the incidents and the great suffering experienced from repeated refilling of the abdomen with fluid and the necessarily repeated tappings, surely justify the attempts toward relief by any methods short of cruel or painful procedures. Omentoplexy described by Talma forty-two years ago and modified by Morrison, Babler and others, for various reasons has fallen into disuse time and again, only to be resurrected by those who have taken the trouble to study its limitations and advantages.

"The discovery of insulin, the vagus substance regulating the glycogen synthesis in the liver cells" has given us a second great and good weapon in our fight

against hepatic cirrhosis and ascites of the portal variety.

I wish to report an arrested case of cirrhosis of the liver receiving the benefits of both omentoplexy and insulin injections:

## CASE REPORT

M. K., a white male, age forty-one years, was admitted to the Schumpert Sanitarium August 5, 1939, with delirium tremens. He had been a constant and continuous gin drinker for a number of years, which culminated in the condition for which he entered the sanitarium. He was restrained with considerable difficulty and after the usual sedative treatment his mental condition was relieved. Examination revealed apparently normal heart and lungs. The blood pressure was 130/90, pulse 90, respiration 20, temperature 98°F. The liver was enlarged, extending from the ninth rib to below the level of the umbilicus. Hemorrhoids were large and the anus was everted. The abdomen was filled with fluid. The surface veins of the abdomen were not prominent. There was no edema of the extremities and no puffiness about the eyes. There were no signs of jaundice, the sclera being clear or very slightly yellow-tinged. A low fluid intake, high carbohydrate-protein and low fat diet was instituted. Salyrgan and ammonium nitrate were administered over a period of five days with negative results. He was tapped August 10, 1939, and a gallon of fluid was obtained. Thereafter he was tapped every five to seven days, increasing amounts of fluid being obtained each time.

On September 1, 1939, the Babler modification of the Talma operation was performed under local anesthesia. The abdomen was opened in the median line between the ensiform cartilage and the umbilicus. A large quantity of

clear light fluid was evacuated. The liver was visualized and was observed to be of the hob-nail variety. The omentum was very large, thick and broad. There were no adhesions encountered. The omentum was brought through an opening in the peritoneum, spread out, and attached by means of several plain catgut sutures to the undersurface of the muscles. The sheath was closed with chromic catgut and the skin with interrupted silkworm gut. There was no shock. The patient was absent from his room just thirty minutes. The skin sutures were removed on the twelfth day. There was no infection, however, the patient's abdomen continued to fill rapidly. It was necessary to tap him every five to seven days when as much as two gallons of fluid were usually obtained. On December 28, 1939, he was tapped for the last time. At several tappings previous to this date it was noticed that the amount of fluid obtained was being gradually diminished. From then on the fluid was controlled with salyrgan and theophylline intravenously and ammonium nitrate by mouth. On December 14, at the suggestion of Dr. Lloyd, 5 units of insulin three times a day was started. The results were highly satisfactory. The patient's appetite improved and the ascites gradually disappeared after three weeks use of insulin so that by February salyrgan was no longer necessary. He was discharged from the hospital February 28, 1940. At the present time he is back at work as a salesman in a furniture store. He still adheres to his diet and the insulin and refrains from gin. There has been no recurrence of the ascites and no salyrgan, theophylline or ammonium chloride have been used since his discharge from the sanitarium. It is not uncommon for the fluid to cease to accumulate after repeated tappings, presumably because of the establishment of venous anastomosis at the site of the puncture.

Therefore, I do not presume to say that the operation could be the only reason for the relief of the ascites. According to Warbasse-Smythe, improvement should be secured in 90 per cent of patients operated upon if the operation is done before the health of the patient is seriously impaired. The operation usually fails in cases of chronic congestion of the liver. In Laennec's or portal cirrhosis which is characterized by an absence of jaundice and pathologically

by undisturbed liver cells and large biliary ducts, the operation is indicated. According to A. Blod, 40 per cent of cirrhosis of the liver operated upon by this method, are relieved of the ascites. The reason for the failure in the other 60 per cent of the operations is that the operation has been improperly used. An absence of jaundice and adhesions, and a large omentum insure the success of the operation.

The original operation first described by Talma\* was best performed under a general anesthetic. The upper surface of the liver was rubbed with gauze for the purpose of irritating its peritoneal covering and causing it to become adherent to the diaphragm. The peritoneum in the neighborhood of the surgical incision was rubbed and the omentum sewed to the irritated surface. Bickham advocated the use of a brush generally used in preparing the hands for operation for the irritation procedure, and also irritating the serous surface of the spleen as well as the liver.

E. A. Babler and others have modified the operation which can be done under local anesthesia, the operation which I have described in the report of my case.

The adhesions which form as a result of the operation cause anastomosis between the veins of the mesenteric system and those of the anterior abdominal wall; and blood from the veins of the abdomen is carried to the vena cava without passing through the portal veins and liver. This process takes from four to six months before results are noted. Subcutaneous drainage for ascites has been attempted by many methods; silk thread, glass tubes, silver wire tubes of fascia, skin, serous membrane have all been used. Anastomosis of the saphenous vein with the peritoneum was performed by Rontte. According to Warbasse, while the reports from a few cases show good results, the operation probably has no permanent value. P. Rosenstein has described a valve-like opening in the urinary bladder. Anastomosis between the vena cava and the portal vein, between

\* Berlin klin. Wochenschr., September 19, 1898.

the superior mesenteric vena cava and between the superior mesenteric and the ovarian veins have also been suggested. But the Talma operation and its modifications appear the most practical surgical procedure for the treatment of ascites due to hepatic cirrhosis. Detiverlier says that the "Talma operation has been more or less successful in certain cases in encouraging anastomotic circulation."

E. L. King who has collected 227 cases reports the following:

	No.	Per Cent
Deaths.....	75	33
Failures.....	34	15
Improvements.....	29	13
Cured.....	84	37.3

Walter Hughson reports twenty-eight cases as follows:

Peritoneum and liver scrubbed..	9
Liver painted with iodine.....	1
Omentoplexy.....	12
Cholecystomy.....	2
Splenectomy.....	1
Simple Iaporatomy.....	1
Reaccumulation of fluid.....	17
Known to be dead.....	16
Survived average.....	22 days

Arthur Tempsky reports twenty-five cases of which thirteen were hypertrophied, eight atrophic cirrhosis and one cardiac cirrhosis showed marked improvement for a long time. Three cases lived twelve, five and four years, respectively. The one that lived twelve years was tapped after two years.

Strobel who reports eight cases had two cures, both hypertrophic cirrhosis. Simon who has collected 224 cases is of the opinion that hypertrophic cirrhosis offers the more favorable prospects for satisfactory results. Bickham, quoting Moynihan, states that the most favorable cases for operation are those in which the liver is enlarged rather than atrophied. Munkowski is also of the opinion that in hypertrophic cirrhosis the results are much better than in the atrophic

variety. Practically all surgeons who have had experience with this operation are in agreement that the operation should be performed early and not as a last resort. Talma has suggested that a patient should not even be tapped before the operation is performed. In the Hanot (primary) and the Chacot (obstructive) cirrhosis, the operation should never be attempted. Diabetes, heart disease, tuberculosis and nephritis and contraindications for the operation. In recent years the operation has fallen into disuse probably because the indications and contraindications were not so well understood. Talma only advised the operation when the liver cells were not impaired greatly. Icterus, urobilinuria, acholia, hypocholia of the feces, xanthoma and pigmentation of the skin were signs according to Talma that precluded success for the operation. Simon who, as I have stated, previously collected 212 cases reached the same conclusions as Talma had reached, that is, that the operation should be performed at the first signs of ascites and then only when the cirrhosis is of the portal type.

The use of insulin in the treatment of cirrhosis of the liver is not new. From time to time there have appeared reports of the successful use of insulin in this disease. McCabe and Hart reported five cases in 1933. Walker and Wood reported a most unusual result with insulin in 1935, while F. Hart and J. R. Lisa have recorded an arrested case verified by autopsy, the patient having died of an acute attack of pneumonia unrelated to the chronic condition with which he was afflicted.

I have been unable to find a single instance recorded in which the patient has had the benefit of both the Talma operation and the routine use of insulin and high protein-carbohydrate diet. I am not unmindful of the fact that the successful issue in one case is by no means conclusive proof of the efficacy of treatment. Indeed, scattered throughout medical literature one finds many reports of cases of ascites arrested as the result of various procedures, but the happy results reported from time

to time as the result of the use of either procedure used in this particular case, certainly places their combination upon a sound and practical foundation. It is hoped that others will try out this method for the treatment of a condition which for some time has been considered hopeless by many students of the problem.

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OCCASIONALLY, signs of acute hepatic insufficiency, may occur in the absence of obvious signs of portal obstruction. In such instances the liver failure is often precipitated by some toxic agent such as morphine, alcohol, or a coincidental infection.

# TOTAL GASTRECTOMY

## REPORT OF TWO CASES

LON GROVE, M.D.

AND

E. A. RASMUSSEN, M.D.

Associate Professor of Surgery,  
Emory University Medical School

Surgical Resident, Emory University Hospital

ATLANTA, GEORGIA

WHILE total gastrectomy is still not a common procedure, during recent years there has been an increasing number of successful cases reported, and there are probably others which have not appeared in the literature. It has frequently been urged that this be done, hence we are reporting two additional cases.

The scirrhus form of carcinoma,<sup>3</sup> generally spoken of as the leather bottle stomach is generally accepted as the ideal lesion necessitating total extirpation. This is because of its slow growth, and the relatively rare extragastric metastasis, until the last stages of the disease. It was this type of lesion that necessitated total gastrectomy in the two cases being reported. In each case the growth involved the entire stomach, except for a small portion at the cardia, and in neither case was there gross evidence of involvement of the surrounding tissues or lymph-nodes. Upon entering the hospital neither patient showed evidence of marked anemia or malnutrition and both were considered good operative risks.

Case I is now fourteen months postoperative and, during this time, the patient has eaten well, has had no marked digestive difficulty or epigastric distress, and there has been no diarrhea, except on one occasion; and she has not shown marked macroscopic anemia. She has recently begun to lose weight and we believe shows evidence of recurrence.

Case II is now three months postoperative. She is taking four small meals daily without discomfort or diarrhea, has shown no anemia to date and is gaining weight.

The technic employed is a modification of those described by Lahey, Graham and others. The night before, and the morning

of operation, the stomach is thoroughly lavaged with .5 per cent dilute hydrochloric acid, and the Levine tube is left in the stomach.

In both cases the operation was performed under nitrous oxide-ether anesthesia. A high midline incision, from the ensiform to a point approximately one-half inch below the umbilicus, was found to be satisfactory, and it was not necessary to carry out cartilage or rib resection or to enlarge the incision in any manner. After the stomach had been completely mobilized, by ligating the gastrocolic and gastrohepatic attachments, the duodenum was cut across between clamps, with cautery, and the end inverted in the usual manner. At this time the Levine tube is withdrawn to such a position that the tip lies in the distal end of the esophagus and continuous suction is applied so that any mucus in the esophagus is aspirated while the anastomosis is being performed. Using the stomach for traction, the esophagus is freed from the diaphragm, by turning up an anterior and posterior flap of the serous coat of the diaphragm, and by so doing, cutting the right and left vagus nerves, freeing the esophagus which can be drawn down for a distance ample for resection and anastomosis. A long jejunal loop is next brought through a rent in the transverse mesocolon and sutured to the diaphragm with interrupted sutures of silk, as the first layer of the posterior suture line. We placed the loop postcolic because we believe that there is less drag than when it is placed anticolic, which results in less tension on the anastomosis and, therefore, causes less pull on the anastomosis. The esophagus is now cut across and an esophagojejunos-

tomy is performed using No. 000 chromic catgut as suture. The flaps of the dia-phragmatic peritoneum are now turned

ings every two hours. By the fourteenth day, the equivalent to a soft diet is begun. This is given as small feedings five times



FIG. 1. Case 1. Illustration of stomach showing diffuse scirrhus carcinoma.

down and sutured to the jejunum below the line of anastomosis. This point in technic has been emphasized by Lahey,<sup>1</sup> as serving two purposes: first, to overlap the line of anastomosis thereby reinforcing it; second, to act as stay sutures relieving the pull or strain on the anastomosis; an enter-enterostomy is now performed between the limbs of the jejunal loop. This has been done for two reasons: first, to encourage rapid emptying of the proximal loop, in order to lessen the weight on the anastomosis; second, to prevent regurgitation of bile into the esophagus.

The Levine tube remains in the esophagus for the first five postoperative days, and is aspirated at frequent intervals, and nothing is allowed by mouth or through the tube, nutrition being maintained entirely by the use of intravenous fluids, with the addition of concentrated vitamins. Jejunostomy, as advocated by some, was not employed in either case.

On the morning of the sixth postoperative day, the tube is withdrawn, and water, milk and lime water are given so that the patient receives a small amount each hour. These are continued until the tenth day, when fruit juices, cream of wheat, strained oatmeal and a soft boiled egg, in small amounts, are added to the diet. The patient, by this time, is receiving small feed-

daily. Before dismissal from the hospital, the patient is taking four small meals daily without discomfort, along with vitamin therapy and desiccated pig's stomach. The postoperative course in both cases was surprisingly smooth and without complications.

#### CASE REPORTS

CASE 1. A woman, age forty, was seen at the Winship Clinic September 10, 1940, at which time she complained of epigastric discomfort for a duration of one year. The dull epigastric pain usually followed meals and the swallowing of only very small amounts of liquid resulted in a sensation of extreme gastric fullness. She had noticed no tarry stools. She had lost approximately thirty pounds weight during six months prior to admission. Family and past history were negative.

Laboratory studies revealed erythrocytes, 4,000,000, hemoglobin 65 per cent, leukocytes 4,800, negative urinalysis and negative blood Kahn. Gastric analysis revealed fifteen degrees total acidity, no free hydrochloric, one plus lactic acid and one plus blood. X-ray diagnosis of scirrhus carcinoma of the stomach was made.

Total gastrectomy was performed September 18, 1940. The pathology department reported infiltrating mucoid carcinoma of the stomach.

On September 23, 1940, erythrocytes numbered 3,200,000, hemoglobin was 55 per cent, and leukocytes numbered 4,600. October 2,

1940, blood analysis revealed 3,500,000 erythrocytes and 58 per cent hemoglobin. December 14, 1940, erythrocytes were 3,700,000 and

the dull epigastric ache and nausea. She vomited at irregular intervals but gave no history of hematemesis. There had been no

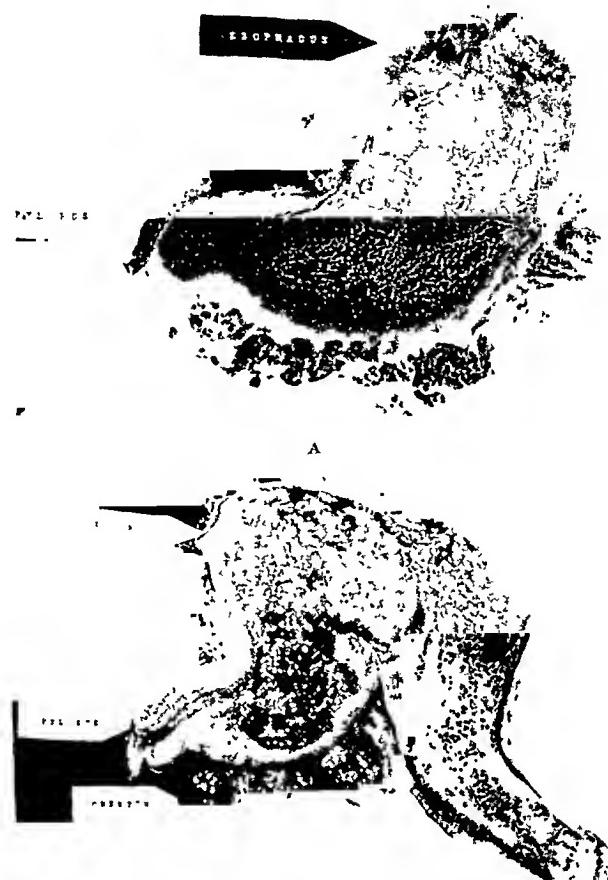


FIG. 2. Case II. A and B, illustrations of stomach and omentum showing diffuse scirrhus carcinoma.

hemoglobin 66 per cent. January 17, 1941, erythrocytes numbered 4,400,000 and hemoglobin 82 per cent.

This patient has now been living more than one year and for most of this duration has been comfortable. She had one attack of diarrhea with cramping two months after leaving the hospital, which lasted for four days. She has now lost considerable weight, has developed some ascites and in all probability has a recurrence.

CASE II. A woman, age forty-seven, was seen at the Winship Clinic July 29, 1941, at which time she complained of a dull ache in her epigastrium accompanied by nausea which seemed to come on more commonly when her stomach was empty. These symptoms had persisted for four months prior to the time at which she was seen. Food seemed to alleviate

tarry stools. She had had considerable belching, her appetite had been poor and she had lost eighteen pounds weight during three months prior to admission. Family and past history were negative.

Fluoroscopic and serial film studies of the stomach revealed a persistent filling defect involving the upper two-thirds of the stomach and lower esophagus. The appearance was that of a scirrhus carcinoma of a *linitis plastica* type.

Due to the extensive type of lesion which apparently involved the esophagus and to the fact that the growth might have been a lymphosarcoma, she was given deep x-ray therapy.

She returned to the clinic August 25, 1941, at which time x-ray studies revealed no change in the appearance of the lesion so she was

admitted to the surgical service for esophagogastrchoscopy and possible total gastrectomy. Esophagoscopy, August 25, 1941, by Dr. Wright, revealed no esophageal lesion and a biopsy from the gastric fundus just beyond the cardia demonstrated chronic inflammation of the stomach wall.

The laboratory reported erythrocytes 4,200,000, hemoglobin 75 per cent, leukocytes 7,300, negative urinalysis and negative blood Kahn.

Total gastrectomy was successfully performed August 30, 1941. The pathology department reported scirrhous carcinoma of the stomach with diffuse wide spread infiltration of the gastric wall. On September 8, 1941, erythrocytes numbered 4,480,000, and hemoglobin was 80 per cent. September 24, 1941, erythrocytes were 4,600,000 and hemoglobin 92 per cent. To the present time she has had no epigastric distress, feels much better than formerly, her general condition is satisfactory and she is gaining weight slowly.\*

\* This patient returned to the clinic on November 19, 1941, at which time she appeared well and had no complaints. The blood count showed 3,900,000 red cells and 78 per cent hemoglobin. She was taking a soft diet well without discomfort. X-ray showed the anastomosis functioning well and a chest plate was negative for metastasis.

#### SUMMARY

Two cases have been presented in which total gastrectomy was successfully performed. A diagnosis of linitis plastic type of scirrhous carcinoma of the stomach was made in each instance and in neither case was there gross evidence of extragastric metastasis although gastric symptoms had persisted, for one year and four months, respectively.

Both patients recovered from the operation with surprising ease and within two weeks were taking soft foods without discomfort.

We know that these cases are more comfortable following total removal of the stomach and that their general condition improves, therefore, it is not beyond hope that some may be cured by such a procedure.

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# DELAYED SPLENIC RUPTURE

## REPORT OF A CASE

HENRY N. HARKINS, M.D.

Associate Surgeon, Henry Ford Hospital

DETROIT, MICHIGAN

THE importance of traumatic injuries of the abdomen is especially to be emphasized in these days of national emergency. Any data pertaining to and clarifying the nature of such emergencies

TABLE I  
RELATIVE FREQUENCY OF TRAUMATIC RUPTURE OF THE SPLEEN IN A SERIES OF SUBCUTANEOUS ABDOMINAL INJURIES

Author	Year	Percentage of Splenic Ruptures
Mazel	1932	30
Bronaugh	1935	33
Wright and Prigot	1939	48
Average		37

TABLE II  
COMPARISON OF MORTALITY OF OPEN AND CLOSED INJURIES TO THE SPLEEN  
(After Maes and Rives, 1941)

Type of Case	No. of Cases	Deaths	Mortality, Per Cent
1. Open (gun shot wounds).	11	10	91
2. Closed, total	26	9	35
a. Auto accidents	11	6	55
b. Falls	11	2	18
c. Miscellaneous*	4	1	25

\* Run over by wagon, struck by bicycle, fist fight, and struck by iron pipe, each one case. The first of these listed died while the other three recovered.

are now of vital consequence. Of all serious subcutaneous intra-abdominal traumatic injuries, splenic rupture heads the list. The percentage of such injuries that involves the spleen has been variously stated by different authors as shown in Table I. Rupture of the spleen, at least in civilian life, is about twice as common from closed

as from open abdominal injuries as shown in Table II, but this preponderance of the former is less evident in war injuries.

The occurrence of delayed splenic rupture is important and should be recognized by all those treating traumatic patients. This syndrome has been neglected in the literature and is undoubtedly more common than is realized. McIndoe (1932) collected forty-six cases, while Steenrod (1940) added eight additional cases, bringing the total to fifty-four. Wright and Prigot (1939) reported two cases while Fey and Turow (1941) reported one. This makes a grand total of fifty-eight cases of delayed splenic rupture, including our own case. The following case report is made to stimulate interest in this syndrome:

### CASE REPORT

O. M., a white male, aged forty-eight, employed as a millwright foreman, previously in good health, was in an automobile accident on November 18, 1940. He was unconscious for a few minutes and when he regained consciousness complained of a headache, soreness in the left knee and a "wrench" of the left side, in the region of the lower ribs in the midaxillary line. Of the three complaints, the headache and pain in the left knee were the most severe. However, because he felt tired and "washed out," he remained in bed most of the time during the ensuing four days.

At about 11 P.M. on November 22, 1940, the patient became very pale, his pulse became very weak and when a physician who was called examined him his blood pressure gradually dropped during the three-hour interval until he was brought to the Henry Ford Hospital in an ambulance.

On admission at 2 A.M. on November 23, 1940, the patient appeared quite pale. The blood pressure was 80/50, the pulse 120, and

the red count was moderately reduced. The urine was normal. Physical examination was essentially negative except for the abdomen and the generalized pallor, arterial hypotension and tachycardia. The abdomen was moderately distended and tense with generalized rigidity and tenderness, most marked in the left upper quadrant. A diagnosis of possible ruptured spleen was made and operation performed at 3 A.M., one hour after admission, under ethylene-ether anesthesia.

*Operation.* A left paramedian incision was made from near the costal margin to the level of the umbilicus. On opening the peritoneal cavity a large amount of free blood was found. To expose the region of the spleen more easily, a left lateral transverse projection of the longitudinal incision was made for a distance of 11 cm. from the lower end of the latter. On freeing loose fibrinous adhesions around the spleen, still more blood welled up and it could not be definitely ascertained whether this represented fresh bleeding or merely release of a partially encapsulated hematoma. At any rate, there was a marked flow of blood up into the wound estimated at 1,200 to 1,500 cc. Because of the urgency of the situation a plasma transfusion was begun. The spleen was felt to be intact, except for a rent in the capsule about one or two inches long on its convex surface, and already partially freed from its diaphragmatic attachments. It was further rapidly mobilized by incision of the posterior layer of the lienorenal ligament and the pedicle constricted by wrapping a Mikulicz pad around it, the left hand maintaining compression. This method of stopping bleeding from the ruptured surface of the spleen was quite effective, but had the disadvantage of leaving little room to ligate the pedicle. Finally, the main artery and vein were separately ligated with No. 0 chromic catgut and the spleen was removed. A few small bleeding points along the gastrolienal ligament and its reflection onto the diaphragm were ligated. No further exploration of the abdomen was made except to note that the liver, stomach, duodenum, and gallbladder all appeared grossly normal. The gallbladder was not felt, however.

The abdomen was closed without drainage or retention sutures. A continuous suture of No. 0 chromic catgut was used for the peritoneum and posterior sheath of the rectus, while interrupted far-and-near mattress sutures of the

same material were used for the anterior sheath, and the skin was closed with interrupted silk sutures.

*Postoperative Course.* At the end of the operation, after administration of 200 cc. plasma, the blood pressure was 100/65 and the pulse 100. Immediately on return to his room the patient received 300 cc. more plasma and the blood pressure gradually rose to 125/75. He developed an atelectasis which was treated by bronchoscopy and he left the hospital three weeks after admission. Of interest is the fact that two months later he was admitted to the hospital (February 6, 1941 to March 4, 1941) with what apparently was catarrhal jaundice. At no time was there evidence of portal thrombosis.

*Pathologic Examination.* The spleen measured 18 by 8.5 by 4 cm. and weighed 285 Gm. The capsule was smooth except for some adhesions over the convexity and a point of rupture 2.5 cm. in length on the convex margin opposite the notch. Considerable clotted blood was attached to the surface and a hematoma 3.5 cm. in diameter was present under the capsule at the site of rupture. On section this rupture extended into the substance of the spleen for a distance of 4 cm. and the tract had a diameter of 1.5 cm. The remaining splenic tissue showed a normal architecture with normal follicles and no degenerative change. Microscopically, no inflammatory reaction was seen and the rupture and hematoma were demonstrated.

*Postoperative Treatment.* The occurrence of portal thrombosis is a frequent complication according to Murray (1941) while Maes and Rives (1941) stated that "the common fear of portal thrombosis seems to be unfounded." This patient received heparin intravenously during his postoperative course and there was no evidence during the hospital stay of any portal thrombosis. The attack of catarrhal jaundice occurring two months after discharge may or may not have been a part of such a syndrome. No evidence of ascites was present at any time after operation.

#### COMMENT

*Diagnosis.* Maes and Rives (1941) have aptly said that "there is no pathognomonic picture of rupture of the spleen." However, when it is remembered that this is the most common, serious, subcutaneous abdominal

injury, it must be thought of whenever evidences of shock, hemorrhage and peritoneal irritation follow severe injury. In instances of ruptured viscera, the elements of shock and hemorrhage, even though present, are not so dominant while the signs of peritoneal irritation are more prominent. Wright and Prigot (1939) advised paracentesis in cases of splenic rupture, obtaining positive evidences of intraperitoneal bleeding in thirteen of fifteen cases. I would tend to agree with Maes and Rives (1941) that in cases of doubt an exploratory incision is preferable to blind paracentesis. In one such case of mine even the exploratory incision did not at first reveal blood, the latter only appearing when the hand was placed in the peritoneal cavity. When this was done, a large volume of blood welled up into the wound.

TABLE III

FREQUENCY OF DELAYED SPLENIC RUPTURE ACCORDING  
TO LATENT PERIOD IN FIFTY CASES\*

Latent Period in Days	No. of Cases
2 to 6.....	24 (48%)
7 to 11.....	14 (28%)
12 to 16.....	5
17 to 21.....	4
22 to 26.....	1
26 to 30.....	1
More than 30 days.....	1
Total.....	50

\* This table includes forty-nine cases reported in the literature, as well as the author's case.

*Time of Rupture.* As shown in Table III, delayed rupture may occur more than thirty days after the original injury. Most of the cases happen, however, during the first eleven days, 78 per cent of instances occurring during this interval and two-thirds of these occur during the first six days.

*Treatment.* The only treatment is prompt operation with adequate shock therapy. In a series of forty-five reported cases with operation, the mortality was 25 per cent. It is probable that the use of more modern methods including adequate doses of whole blood or plasma would markedly reduce this figure.

#### SUMMARY

A case is reported of delayed splenic rupture occurring four days after the original trauma of an automobile accident. A study of fifty-eight such cases indicates that approximately 50 per cent occur during the first week after injury and about 25 per cent additional during the first half of the second week. Prompt operation with splenectomy supported by adequate blood or plasma transfusions is the procedure of choice. The importance of this traumatic injury in wartime is emphasized.

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# CHONDROBLASTIC MENINGIOMAS\*

JOSEPH H. SIRIS, M.D.

Assistant Neurological Surgeon,  
Queens General Hospital

AND

ALFRED ANGRIST, M.D.

Pathologist, Queens General Hospital

JAMAICA, NEW YORK

ONE of the most favorable, but perhaps the rarest of intracranial new growths is the intradural chondroma, which because of its location has been accepted by Cushing and Eisenhardt as one of the meningioma group. An idea of the incidence of this tumor is afforded by the fact that it occurred but once in their series of 306 meningiomas.<sup>1</sup> When one considers the fact that meningiomas comprise about 10 to 15 per cent of intracranial tumors and that the latter in turn occur in less than 2 per cent of autopsies on tumor cases, it is evident that this type of growth is rare. Nevertheless, a sufficient number of reports have appeared to establish this lesion as a distinct clinical entity. The report of de Busscher,<sup>2</sup> in 1939, mentioned sixteen previous cases of cerebral convexity chondroma noted in the literature. To these should be added the basal tumor of Cushing and Eisenhardt and the two intraventricular chondromas reported by Letterer.<sup>3</sup> The former case, though differing from the others in its basal location, appears to belong to this group rather than to the basal chondromas and osteochondromas of bone for no bony attachment could be demonstrated. This growth presumably took origin from the outer end of the superior petrosal sinus. Since the choroid plexus arises as an invagination of the primitive leptomeninx into the attenuated ependymal surface of the primary brain vesicles, such tumors occurring within the ventricles can be considered as of meningeal origin, and therefore as a variant in this group.<sup>4</sup>

Chorobski, Jarzymiski and Ferens<sup>5</sup> carefully culled the literature in reporting a

case in which operation was successful, bringing the total number of instances of intracranial chondromas and osteochondromas to twenty-five. Among the previously reported cases, both osteochondromas and chondromas have been noted, with the pure chondromas more numerous. Two were sarcomatous lesions or at least recurrences.<sup>1,6</sup> It is of importance that these tumors be distinguished from other reported cases<sup>7,8</sup> of chondromas of the base of the skull secondarily involving the brain, where the tumor is extradurally situated and arises from bone. The origin of such cartilaginous growths is more easily explained than that of the intradural variety.

As has been pointed out, however, this type of tumor is not limited to the convexities. Regardless of site, all have in common a meningeal attachment. They are encapsulated, and although they compress the brain markedly, do not invade it, unless sarcomatous change is present. Occasionally, the dura overlying the tumor is in turn firmly attached to the skull.

The following case is the twenty-sixth of its kind recorded in the literature, the sixth in which complete, successful removal of the growth was carried out:

## CASE REPORT

CASE 1. (Q. G. H. #A26903). J. M., an eighteen year old white male, was admitted to the Queens General Hospital on January 16, 1941. He complained chiefly of convulsive seizures of four months' duration. There was a total of five paroxysms during this period. With one exception they were all of a completely generalized pattern, without aura, comprising tonic and clonic features and lasting about twenty minutes. The second attack

\* From the Departments of Surgery (Neurosurgical Division) and Pathology, Queens General Hospital, Jamaica, Long Island, N. Y.

appears to have been initiated by a feeling of stiffness in the right upper limb which subsequently went on to a generalized seizure. Both



FIG. 1. Radiograph of skull showing ovoid, mottled, calcified tumor shadow.

the patient and his mother were aware of a progressive inability on his part to concentrate satisfactorily on his school work for the previous five years. For about a year prior to admission it had been observed that the patient was inclined to be more irritable than was his custom, became increasingly wayward and would stay out exceptionally late at night. An intermittent droop of the right upper eyelid had been noticed during the nine months' period prior to admission.

The patient played a considerable amount of football since the age of twelve. In the course of play he sustained numerous injuries to the head, to which little attention was paid. The injury would, as a rule, daze him momentarily, after which he would continue to play. A month before the development of his seizures he was assaulted and apparently struck on the head, following which he was unconscious and drowsy for about three hours. Subsequently, however, he was able to be up and about in his customary manner.

Examination revealed nothing of significance with respect to the systemic status. Neurologically, one could demonstrate no frank abnormality, apart from an evident psychomotor retardation of slight degree. Otherwise, there was no disturbance of affect, memory, orientation, speech function, cranial nerve innervations, co-ordination, sensation, reflexes or motor power. The patient was right-handed.

*Laboratory Data.* These showed nothing of particular significance in the blood count, serology, blood chemical studies or urinalysis.



FIG. 2. Air studies showing displacement of ventricles by rounded, calcified tumor mass.

Cerebrospinal fluid study revealed clear, colorless fluid under a pressure of 170 mm. of water with no cells and a protein of 40 mg. per 100 cc.

X-rays of the skull revealed an elliptically-shaped, well demarcated, calcific shadow, situated within the intracranial cavity on the right side, near the inner table of the skull and measuring  $2\frac{1}{2}$  by 2 inches. (Fig. 1.)

Since the clinical picture suggested that the shadow noted by x-ray might represent calcification within an old hematoma, it was decided to ascertain this possibility through visualization of the ventricular system. Accordingly, pneumo-encephalographic study was carried out. This revealed an appreciable shift of the lateral and third ventricles to the left, without much distortion of the ventricular system. (Fig. 2.) The normal convexity of the roof of the right lateral ventricle was not appreciably altered. This combination of data suggested that a calcified hematoma was unlikely and that the lesion was in all probability an astrocytoma.

*Operation.* A right lateral osteoplastic craniotomy was carried out under avertin-ether anesthesia. While the bone flap was being

reflected, it was found quite adherent to the dura mater along the groove of the middle meningeal artery. The dura in this region was

not unlike the aura of the second of the patient's convulsions. No convolution appeared on this occasion, however. Both the patient and



FIG. 3.

FIG. 3. Tumor mass (halved by longitudinal section) showing coarse lobulation and finer linear cerebriform superficial gyration.



FIG. 4.

FIG. 4. The lateral and medial aspects of sectioned tumor. The lateral aspect shows the surface lobulation and gyration and the attached dura. The medial aspect shows the central cavity and the encircling zone of more opaque and congested and somewhat hemorrhagic zone of calcification.



appreciably thickened and it was evident that a tumor mass firmly adherent to it, lay directly underneath. Opening the dura revealed a tumor, the size and shape of a lemon, in the Rolandic zone. This was largely covered by brain, but nevertheless extracerebral. It was white, glistening, hard, and had a cerebriform

his associates were aware of steadily increasing alertness in him. At the time of discharge it appeared that he had attained his former mental state.

*Pathological Report. Gross Description:* The specimen (Fig. 3) consisted of a lemon-shaped mass measuring 7 by 4 by 4½ em. and weighed 90 Gm. The external surface was irregularly nodular and lobulated in appearance and very firm. On one surface, a flattened membrane composed of opaque, grayish, fibrous tissue suggested dura and showed some hemorrhage. Four silver clips were seen around the periphery. The tumor mass was firmly adherent to the inner surface of this membrane. The inner surface of the fibrous tissue membrane was reflected over the presenting surface of the large tumor mass, but was firmly adherent as an integral part of the exposed surface.

The mass, on section, (Fig. 4) was composed of a dense wall 1 cm. in diameter, irregular in outline, with a central cystic cavity 4½ by 2 cm. The wall was composed for the most part of a translucent, opalescent, firm, bluish-gray tissue resembling cartilage. A centrally placed encircling rim of calcified tissue which grated and cut with difficulty divided the wall into three distinct layers, the opaque zone of calcification appearing in sharp contrast to the translucent peripheral gray cartilage to either side of it. The presence of calcification was confirmed by x-ray. (Fig. 5.)

The cystic cavity was lined by a yellow, glary, thin, transparent membrane through



FIG. 5. Shadow cast by tumor mass in radiograph. Note the central location and the concentric encircling character of the zone of calcification. The central area corresponding to the cyst structure is free of calcification.

convolutional nodularity. The mass with its attached dura was gradually shelled away from the surrounding brain, leaving a deep tumor bed. By the time closure was begun, the brain at this site had re-expanded considerably. A dural defect about 2 inches in diameter was left behind. The dura was sewn to the galea at the bone edge. The bone flap was sacrificed in view of the possible involvement of the inner table. The wound was closed in layers without drainage.

The postoperative course was uneventful, except for an isolated episode on the seventh postoperative day, when the patient experienced a sensation of stiffness in the right hand,

which protuberant cartilaginous nodulations of the wall could be seen. From the wall of the cavity, thin, filmy, yellowish strands projected,

The central cystic cavity showed an outer, rather dense, fibrous, lamellated, eosinophilic coating applied to the cartilaginous tissue and



FIG. 6. Low power microphotograph showing superficial attached dura, wide zone of cartilage with varying degenerative changes, adjacent calcification and true cancellous bone formation on the innermost aspect with included fatty marrow.

FIG. 7 High power microphotograph showing varying character of cartilage cells and their grouping with adjacent calcification and bone formation.

which contained in their webs glary, somewhat viscid, yellowish, mucoid material.

*Microscopic Description:* Microscopic sections (Figs. 6 and 7) showed the major portion of the tumor tissue to consist of hyaline cartilage with areas of degeneration and ossification. The cartilage cells were rather hypertrophied with some zones showing myxomatous material, and other areas showing distinct calcification. Centrally placed degenerative areas showed irregular calcification with transformation to true bone. The matrix separated some cell groups widely. At the periphery only a small island of ossification was seen. Some true fatty marrow without hematopoietic foci was included between the cancellous bony trabeculas.

The attached dural membrane showed some hemorrhage and was closely approximated to the perichondrium-like capsule of the tumor tissue. One small island of cartilage extended into the dural membrane, resembling the manner of extension seen in Pacchianian arachnoidal granulations.

an inner thin, fragile, membrane-like lining. Nondescript loose strands of tissue were found in this area with relatively few cells and no distinctive histological appearance. In multiple sections, no cellular lining was made out delineating the central cavity.

*Pathological Diagnosis:* Dural chondroma with ossification, marrow formation and cystic degeneration.

#### ORIGIN AND CLASSIFICATION

The possible origin of this particular growth has invited considerable speculation and is as yet unsettled. The possibility of origin from cartilaginous rests misplaced during the complex development of the skull has been considered. Their existence within the meninges, however, is somewhat dubious. It is on this basis that Wolf and Echlin<sup>6</sup> question the likelihood of a meningeal origin and suggest the calvarium as a more plausible possibility. In nearly all the reported cases an intradural attachment was demonstrable and in only two<sup>9,10</sup> was

there an evident connection and attachment to bone, suggesting origin from this tissue.

There do exist theoretical possibilities for the meningeal origin of such tumors. Alpers<sup>11</sup> has shown transitions from meningeal fibroblasts to cartilage cells. He assumes that in this variety of tumor, fibroblasts are "activated" to produce cartilage cells. Included in our own histological sections, spindle-shaped cells with other features of cartilage and a surrounding cartilaginous matrix were observed. Persistent young mesenchyme or tangentially differentiated fibroblasts of the meninges may be the source of chondromas attached to the dura, by this theory. In the literature, associated though not demonstrably causative trauma is noted rather frequently.

In some of the hypertrophic Pacchian granulations, a scant matrix with a distinct resemblance to cartilage can often be seen. Most authors accept such cell nests in the arachnoidal granulations as the origin for meningiomas. Complex tumors of cartilage with calcification, bone and fat content are usually basically chondromas with secondary changes, a known propensity of chondromas throughout the body. Calcification, ossification with marrow formation, occasionally with active hematopoietic foci, various stages of degeneration and cyst formation, are all quite common in the general pathological variations of such cartilaginous neoplasms.

The term, intracranial chondroma, is sufficiently noncommittal but does not serve to distinguish this lesion from other varieties, such as those chondromas of the base which definitely arise from bone. Practically all the described cases are of growths in association with the meninges. By this concept, tumors occurring intraventricularly can be considered as of meningeal origin, for reasons already mentioned. For the present, pending further additions to our knowledge of this growth, the suggested chondroblastic meningioma

would appear to satisfy both regional and histologic criteria of classification.

#### CLINICAL CONSIDERATIONS

A preoperative histologic diagnosis of this type of lesion, such as is possible in some other varieties of brain tumor, is not to be expected. The condition occurs in children, adolescents and adults. Its symptoms and signs do not differ materially from those of other types of intracranial tumor. The clinical course may be of long or short duration, the latter probably being more typical of those characterized by sarcomatous elements. The presence of an x-ray shadow does not serve to distinguish the lesion from other types of tumor capable of undergoing calcification, such as the astrocytoma, meningioma or oligodendroglioma. In this particular case the nature of the x-ray shadow suggested an astrocytoma. Considered in retrospect, one might say that the calcification visualized here was exceptional in density and extent. The pneumo-encephalographic picture was of interest in that the distortion and displacement of the ventricular system was considerably less than the large size of the tumor would ordinarily have led one to expect, this being consistent with the presence of a growth of long standing.

The prognosis is a relatively favorable one, complete and successful extirpation of this type of tumor having been carried out in six of the twenty-six reported cases. Its successful removal carries certain considerations based on the nature of the lesion. It is obviously important that the growth be recognized when encountered. This should not be difficult, even with biopsy study not immediately available. The solid, smooth, white, marble-like character of the tumor with its firm dural attachment is practically unmistakable. Frequently, the dura is in turn firmly attached to the inner table of the skull, as was found in this case. The tendency toward recurrence and the occasional presence of sarcomatous change, make necessary a complete removal of the tumor

with its capsule, as well as a liberal portion of dura beyond its attachment to the neoplasm. The same reasons that compel a complete excision of the growth suggest the need for removal of the overlying bone, even if an endostosis cannot be demonstrated.

The dural defect, even if large, need not be repaired, since connective tissue regrowth may be expected. To circumvent the possibility of a cerebrospinal fluid fistula in the presence of a large dural defect, the wound should be closed securely without drainage. Dural hemostasis must, therefore, be thorough and is probably best accomplished by approximation of the dura to the overlying temporal muscle and periosteum at the bone margin.

#### SUMMARY

1. A case of chondroblastic meningioma, the twenty-sixth to be recorded in the literature, the sixth with complete operative removal, is presented.

2. The origin, classification and clinical aspects of this type of growth are briefly discussed.

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# ANORECTAL AND COLONIC MANIFESTATIONS OF SCHISTOSOMA MANSONI INFESTATION (INTESTINAL BILHARZIA)\*

## CASE REPORT

BENJAMIN W. WARNER, M.D.  
NEW YORK, NEW YORK

**S**CHISTOSOMIASIS mansoni is an endemic tropical and subtropical parasitic disease caused by a blood or fluke worm (*Schistosoma mansoni*) which spends part of its intermediate life cycle in a snail. It gains access to its human host in its larval stage from infected water. The larvae penetrate the skin or buccal mucous membrane and then enter the peripheral veins; after passing through the pulmonary circulation they arrive in the systemic circulation and are carried into the superior mesenteric artery and its branches and then into the portal venous system; they feed and grow in the intrahepatic branches of the portal vein. In their mature form the parasites migrate to the terminal tributaries of the superior and inferior mesenteric veins where copulation and egg-laying occurs. The extrusion of the eggs from the venules produces local pathologic tissue changes and systemic toxic manifestations.

The disease is endemic in Egypt, Central and West Africa, the East Coast of South America, the West Indies and especially in Puerto Rico. With increased travel, population shifts, the establishment of military bases in subtropical and tropical climates, parasitic diseases endemic in those areas will be brought to our attention with increasing frequency.

## CASE REPORT

Mrs. D. S., age twenty-six, was born in Puerto Rico and lived there in a rural area, Bonito, until six years ago when she came to New York City. She had been married for five years and had no children. She was first seen in

the gynecology clinic of Beth David Hospital in February, 1941, complaining of sterility and intermittent pain in her left lower quadrant, unrelated to menstruation. A mass in the left adnexa was palpated. In June, 1941, after several months of observation she was hospitalized on Dr. Mortimer Hyam's service. The routine laboratory findings were as follows: hemoglobin 65 per cent, erythrocytes 4,670,000, leucocytes 8,600 with 78 per cent polymorphonuclears and 22 per cent lymphocytes. There were no eosinophiles. Urinalysis was negative. Blood Wassermann: alcohol antigen 1 plus, cholesterol antigen 2 plus.\* A laparotomy was performed by Dr. Moses Lobsenz. A left tubo-ovarian mass the size of a small peach was found and a left salpingo-oophorectomy and appendectomy were performed. The pathologic diagnoses were: chronic salpingo-oophoritis, corpus lutean cyst of the ovary, atrophy and fibrosis of the appendix. In the appendix slight eosinophilic cell infiltration of the muscularis was noted.

Convalescence was uneventful. Upon her discharge from the hospital she returned to the gynecology out-patient department for follow-up care and complained of slight rectal bleeding, pain and itching. She was then referred to the rectal clinic.

Rectal examination revealed an inflamed, tender posterior anal crypt with a posterior fissure-in-ano and slightly enlarged internal hemorrhoids. Sigmoidoscopy revealed a sessile, elevated pea-sized nodule, diagnosed preoperatively as an adenoma, in the mucous membrane of the posterior rectal wall about four inches above the anus and multiple small papillomas in the vicinity of the rectosigmoidal junction.

\* It was learned later that she had been treated for lues several years previously by a private physician who had found a four plus Wassermann reaction.

\* From the Proctology Service of the Department of Surgery, Beth David Hospital, New York City. Dr. Frederie W. Baneroff, Director of Surgery, Dr. I. M. Brenner, Attending in Proctology. Read before the Beth David Hospital Clinical Society November 17, 1941.

There was a small area of granulation tissue 5 mm. in diameter on the anterior rectal wall. The sigmoid above the rectosigmoidal junction appeared normal.

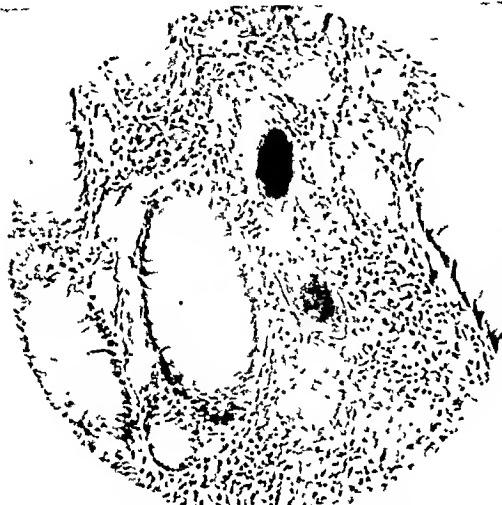


FIG. 1. Section of nodule showing inflammation with mononuclear and polymorphonuclear leucocytes and eosinophiles. Two oval-shaped ova of *Schistosoma mansoni* with a typical lateral spine are seen. (High power.)

The patient was hospitalized again on September 12, 1941. Laboratory findings were as follows: hemoglobin 97 per cent, erythrocytes 4,750,000, leucocytes 8,460 with 72 per cent polymorphonuclears, 27 per cent lymphocytes and 1 per cent monocytes; urinalysis was negative. Stool examination was not done. Under local anesthesia the sessile nodule was removed with the electric cutting loop and the smaller papillomas coagulated; the posterior anal crypt and fissure were excised. Routine histologic examination of the tissue by Dr. Milton Helpern was reported as follows:

"There is a moderate inflammation in the mucosa and submucosa; the inflammatory cells are mononuclear and polymorphonuclear leucocytes and eosinophiles. The sub-mucosa contains dilated venules. In some section there are oval-shaped parasitic ova possessing a typical lateral spine. In one section a group of such ova is surrounded by numerous eosinophiles."

"Diagnosis: chronic inflammation of anal mucosa resulting from infestation with parasitic ova of *Schistosoma mansoni*. (*Schistosomiasis mansoni*)" (Figs. 1 and 2).

With the finding of the ova of *Schistosoma mansoni* the histologic sections of the tube, ovary and appendix previously removed were

re-examined but no ova were found. Unfortunately, the gross specimens had been discarded so that more sections could not be made. The appendix is a fairly frequent site of involvement



FIG. 2. Section of anal crypt showing inflammation and many distorted ova of *Schistosoma mansoni*. (High power.)

and cases of fallopian tube infestation<sup>1</sup> have been reported.

The patient's convalescence was uneventful. She was discharged from the hospital in five days and returned to the clinic. The posterior anocutaneous wound developed excess granulation tissue which was curetted and examined histologically but ova were not found. Sigmoidoscopy revealed the mucous membrane of the rectum and sigmoid studded with punctate bleeding areas which were interpreted as points of rupture or escape of the ova into the lumen of the bowel. Repeated stool and direct rectal smears revealed an occasional distorted ovum.

A blood count on October 10, 1941, revealed: hemoglobin 97 per cent, erythrocytes 4,920,000, leucocytes 11,900 with 59 per cent polymorphonuclears, 28 per cent lymphocytes, 7 per cent eosinophiles, 3 per cent monocytes, 2 per cent basophiles. This was the first appearance of eosinophilia. At this time there were numerous bleeding areas in the mucous membrane of the rectum and sigmoid. There was no diarrhea. A barium enema did not reveal any additional findings in the colon.

A chest x-ray on this date revealed multiple small areas of infiltrations at the right apex which were absent on a subsequent x-ray one month later. It is probable that these infiltration

tions resulted from a *Schistosoma* invasion of the lungs.

At the present writing the patient feels well

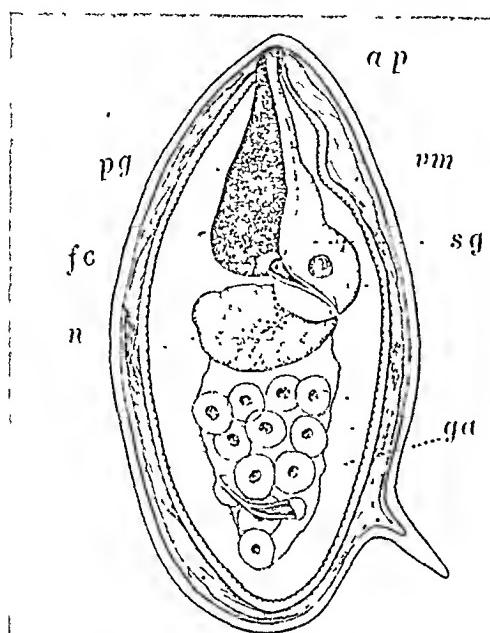


FIG. 3. Typical lateral-spined ovum. (From Faust, after Cort; courtesy of the Univ. of California Press.)

and has no complaint other than slight peri-anal itching. Objectively, the sigmoidoscopic findings persist. The spleen is just palpable but the liver is not. Treatment with fuadin (sodium antimony<sup>111</sup> bisatechol 2.4 disulfonate of sodium) intramuscularly has been started.

The cause of human Schistosomiasis involving the urinary bladder with hematuria as its outstanding symptom was recognized and described by Dr. Bilharz in Egypt in 1851 and this disease bears his name. For many years all types of human Schistosomiasis were called Bilharzia until attention was called, in 1893, by Dr. Manson to the morphologic difference in the ova from an essentially intestinal type of the disease. In this type ova with a lateral instead of a terminal spine were identified. *Schistosoma* producing the lateral-spined ova have a different geographic distribution and produce a different visceral involvement and carry the name of Manson. (Fig. 3.)

The life cycle<sup>2</sup> of the parasites in the vesical and the intestinal type of Schisto-

somiasis are similar differing only in their final localization in the veins of the portal system; both types produce similar pathological changes in the host but in different viscera. *Schistosoma mansoni* eggs are discharged from their human host in feces, occasionally in urine. Careless toilet habits and faulty sewage disposal result in the contamination of bodies of water which are also the suitable environment for a specific species of snail (*P. guadaloupensis*) which acts as an intermediate host. The ovum when discharged in the water liberates a miracidium which enters the snail's visceral mass where it multiplies and grows, giving rise to another intermediate larval stage, the cercariae, which possess a long tail. The larvae in the cercarial stage leave the snail after four weeks and move actively in the water; they can survive from one to three days if they do not find an appropriate human host. On making contact with the exposed skin or buccal membrane of their human host, they penetrate the skin or mucous membrane, their tails drop off and within one-half to one hour they penetrate to the deeper layers. Infestation cannot occur by oral ingestion as the larvae cannot survive the action of gastric juice. From the deeper layers of the skin the larvae enter the peripheral venules, are carried to the right heart and thence to the pulmonary capillaries.

"The larvae having reached the pulmonary capillaries squeeze their way through, enter the left heart, systemic circulation, abdominal aorta and superior mesenteric artery. Only those larvae survive which enter the superior mesenteric artery. Thence they are carried through the capillaries to the superior mesenteric vein and enter the intrahepatic radicles of the portal vein where they feed on red blood cells, become sexually differentiated and mature. On reaching maturity, the adult worms move against the portal blood stream to the ileo-colic and colic branches of the superior mesenteric vein and wander into the anastomoses of the venous circulation toward the lower branches of the inferior

mesenteric vein especially in the hemorrhoidal plexus in the Manson type and in the vesical plexus of veins in the Bilharzia type. This growth and migration of the adult worm takes about six weeks from the time of entrance of the larvac into the skin. In the venous plexus copulation occurs and the female then makes her way into the smallest venule which becomes distended and there deposits her lateral-spined eggs one at a time from one to several hundred per day, moving to a new site for each egg. The distended vein tends to return to normal caliber; the spine of the egg penetrates its wall and by both mechanical and lytic digestive action perforates the vein and is either extruded into the lumen of the viscus, the sub-mucosa or the peritoneal surface or peri-rectal tissues. The eggs discharged into the lumen of the bladder or rectum are excreted in the urine and feces and if a body of water containing an appropriate species of snail is contaminated, the snails become infected and the cycle begins again in the intermediate host.”<sup>2</sup>

The entrance of the larvae into the skin is accompanied by an intense pruritus spoken of by the natives of Puerto Rico as “piquina.” This may last several hours to several days. There is a type of *Schistosoma* in snails in resort lake regions of Michigan and Minnesota which penetrates the skin of bathers and sets up an intense skin rash with itching called “swimmer’s itch”<sup>3,4</sup> but fortunately the larvae in these cases are destroyed in the deeper layers of the skin and do not enter the circulation. There are no reports of cases in residents of the United States who have never left this country. An infection is reported<sup>5</sup> in a resident of the United States who dipped his hand into a home aquarium which contained a species of the snail transmitting the Egyptian type of Schistosomiasis.

With promiscuous distribution of human excreta and improper sewage disposal in the tropics and especially in Puerto Rico where the rural areas are studded with irrigation ditches with stagnant water and

slow moving rivers, as well as lime stone pools offering a suitable environment for the appropriate species of snail, the incidence of *Schistosomiasis mansoni* in the general population is about 12 per cent, while in certain endemic areas the incidence of infestation reaches 50 to 60 per cent.

The clinicopathologic picture and symptomatology are classified by Craig and Faust<sup>2</sup> into three stages: “(1) invasion and incubation period—six to seven weeks; (2) egg deposition and extrusion; (3) tissue proliferation and repair.” A diagnosis is seldom made in the first stage although there may be symptoms of mild toxemia and occasionally diarrhea of supposedly toxic origin. It is during the second stage of egg-laying and extrusion which occurs from five to seven weeks after exposure that local abdominal or intestinal and systemic toxic symptoms make their appearance. There may be a sudden onset with temperature, chills and sweating, abdominal pain with tenderness along the colon, dysentery with passage of blood and mucus with lateral-spined ova in the stool, dry cough and even parenchymatous infiltration especially of the apices, urticaria, enlargement and tenderness of the liver and later splenic enlargement. There is leucocytosis and eosinophilia.<sup>2,6,7</sup>

With subsidence of this acute phase which may have varying degrees of severity, proliferative and reparative tissue changes occur. These granulomatous inflammatory changes depend upon the location of the adult worm and the site of egg extrusion and may appear clinically as superficial ulcerations with granulations, papillomas and pseudo-adenomas (sessile or polypoid). The ova may be extruded to the peritoneal surface of the bowel producing pseudotubercles or into the perirectal tissues with resultant fistulas. Fistulization may occur from any part of the involved bowel. The granulomas in the lumen of the colon and rectum may become polypoid and produce the same sequence of symptoms and complications common to all polyps. Malignant degeneration in the

granulomas is not rare.<sup>2</sup> If the polypoid granulomas are located in the rectum or anal canal, they may prolapse through the anus. The cryptitis is due to the presence of the ova; hemorrhoidal vein engorgement may result from obstruction of the venules by the adult parasites and from interference with lymphatic and venous circulation due to local inflammatory infiltration and obstruction of the portal circulation where liver enlargement and subsequent cirrhosis occurs.

In this connection a report by a Cairo surgeon, M. Samy,<sup>2</sup> on "Bilharzial Piles and Anal Fissure" is interesting: "In the routine examinations and treatment of piles the author has met with a peculiar kind of piles which deserve a special treatment. The patients suffering from this kind of piles are mostly from the country and suffer from all the usual symptoms of piles. Some intelligent patients may give a history of a severe fever, sometimes amounting to 40 degrees C. or more, accompanied by an urticarial rash, acute abdominal pain, rigors symptoms of pulmonary congestion and profuse sweating. This may be accompanied by some diarrhea. After about three months from the fever the local symptoms of piles begin to appear. If they are operated on they recur unless systemic treatment is instituted."

The diagnosis of Schistosomiasis mansoni infestation is made from the history of travel in an endemic area, finding the ova in the stool or peri-anal or rectal swabs,<sup>2</sup> and tissue biopsy. The serologic tests are not developed sufficiently to be of value for general usage as diagnostic aids. In the acute or open stage of active egg extrusion the eosinophilia, urticaria and dysentery may indicate the diagnosis but it is also at this stage that typhoid, tuberculosis and malaria are frequently incorrectly diagnosed. In the proliferative stage sigmoidoscopy may be of great value with biopsy of any granulomatous tissue seen. As the

infection becomes more chronic, eggs in the feces gradually decrease in number.<sup>2</sup>

#### SUMMARY

A case of Schistosomiasis mansoni infestation in a native Puerto Rican, now living in the United States, with predominant anorectal manifestations is reported. Physicians should be on the alert to suspect this infestation in soldiers and workers who return from their stations in Puerto Rico and other endemic areas and present anorectal and intestinal symptoms with or without enlargement of the liver and spleen. Eosinophilia is inconstant and usually absent in the late stages. Pulmonary infiltrations may be confusing unless the infestation is suspected.

While mention of a third type of pathogenic human Schistosomiasis was not intended for this report, it is now pertinent to make note of Schistosoma Japonicum infestation which is endemic in and about China and Japan. This Schistosome involves the small bowel with severe systemic toxic symptoms.

I am grateful to Dr. Milton Helpern and Dr. Alfred Gudemann of the Pathology Department of Beth David Hospital for their kind assistance in preparing this report.

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# A RARE COMPLICATION OF THE MILLER-ABBOTT TUBE\*

LOUIS R. KAUFMAN, M.D.,

Professor of Surgery, New York Medical College

SABATO SERPICO, M.D.

Assistant Attending Surgeon,  
Flower and Fifth Avenue Hospitals

AND

WALTER MERSHEIMER, M.D.

Chief Resident in Surgery, Metropolitan Hospital

NEW YORK, NEW YORK

**T**RAUMATIC edema of the larynx produced by the Miller-Abbott tube is a rare complication and seems worthy of reporting.

As the simple but important steps in the introduction and passage of the Miller-Abbott tube have become more familiar to us, we have come to depend upon its more frequent use for decompression in a large group of cases. These include the more serious acute obstruction but also elective resections, as well as the border-line cases presenting a degree of abdominal distention demanding laparotomy. In this latter group the use of the tube may permit not only valuable preoperative preparation but may even avoid the necessity for intervention.<sup>1-6</sup>

Conservative decompression in intestinal obstruction in contrast to surgical decompression (enterostomy) constitutes an important contribution to the reduction of mortality in this group of cases.

Before the advent of the inlying suction tube, the death rate in intestinal obstruction averaged from 60 to 75 per cent. (Best<sup>7</sup> gives the following figures: Guillame 63.2 per cent; Arhurst 69.3 per cent; Lee and Downes 75.0 per cent; C. J. Miller 61.0 per cent.) Since the advent of the Miller-Abbott tube Whipple<sup>20</sup> states that the mortality has been reduced 50 per cent in intestinal surgery. Johnson, Penberthy, Noer and Kenning<sup>13</sup> have reported a mortality of 25.6 per cent. Of fifty-four patients treated by intubation, five or 9.3 per cent died as a result of intestinal

obstruction, while in the remaining nine who also died, intubation was carried out to relieve distention associated with other conditions which caused death. The University of Minnesota has reported a patient mortality of 17.9 per cent and a case mortality of 14.7 per cent.

In our service, we have employed the Miller-Abbott tube in approximately seventy-five cases. No important complication has followed its use which we believed could in any way be attributed either to the passage of the tube or to its continued use over many days. Few of the patients have complained of any particular discomfort.

C. G. Johnson<sup>15</sup> says that: "The tube occasionally causes irritation to the nose and throat. We had one patient who developed otitis-media during treatment, and another in which there was a rupture of esophageal varices presumably from trauma by the tube." Morawitz and Henning<sup>17</sup> report that some patients complained of pharyngeal irritation which disappeared when a thinner tube was substituted and Morrison states that "cricoid chondritis may occur when a rubber feeding tube has been retained in the esophagus for long periods." O. H. Wangensteen<sup>19</sup> et al. state, "Two patients have been observed with injury of the arytenoid cartilages following prolonged intubation. One of these was our own patient. The other patient was admitted here with edema of the arytenoid cartilages and larynx for which tracheotomy was done." Iglauer and Molt<sup>13</sup> have found that severe injury to the larynx is

\* From the Department of Surgery, New York Medical College, Flower and Fifth Avenue Hospitals and Metropolitan Hospital.

occasionally excited by the presence of the indwelling tube and that this complication may occur after a comparatively brief sojourn of the tube. They have observed ten such cases in two years. Eight of these patients developed laryngeal stenosis of such severity that tracheotomy became imperative. The tube was inlying for comparatively short periods varying from six to twenty days. The average period was eight and a half days. Laryngeal examination in the acute stage revealed evidence of inflammation and edema. The laryngeal inflammation was secondary to the presence of an indwelling duodenal tube. The primary lesion appeared to be due to pressure necrosis of the esophagus at its attachment to the body of the cricoid cartilage.

While some injuries are mild and even escape notice, others are severe enough to jeopardize the life of the patient, and may require an emergency tracheotomy (Wangensteen,<sup>19</sup> Iglauder and Molt<sup>18</sup>).

These injuries of course are not peculiar to the Miller-Abbott tube, but are common to any suction tube, as the casual factor is trauma. These injuries we believe would be more common were they looked for, but as Wangensteen<sup>19</sup> writes: "In as much as our pathologists do not examine routinely the nasopharynx, larynx and upper reaches of the esophagus, it is of course not likely that in this region, where such pressure effects are most likely to arise, several have escaped notice."

#### CASE REPORT

M. G., a seventy-eight-year old Spanish, white female, was admitted to the Metropolitan hospital on May 7, 1941.

Her chief complaint on admission was vomiting and generalized abdominal pain of three days' duration. Vomiting was green and followed each meal; pain was severe and colicky radiating to the right shoulder. The patient was a regular user of cathartics. No blood or mucus was found in the stools. An enema taken the night before admission was ineffectual. The important point in her past history was the fact that the patient was treated in another

institution four years ago for "stone in liver" but was not operated upon because of poor general condition.

Physical examination revealed a white female, small of stature and somewhat obese, but apparently not acutely ill. The abdomen was distended and soft with slight tenderness throughout which was more marked over the right upper quadrant. Peristaltic sounds were heard with tympany. No rigidity, succussion splash, scarring or hernia were present. Rectal examination revealed no feces on the examining glove, or any intrinsic pathological condition. Tachycardia and moderate myocardial damage with generalized senile arteriosclerosis were present. One independent finding was that of an asymptomatic adenomatous thyroid.

Laboratory findings were as follows: The urine was negative; Wassermann and Van den Bergh tests were also negative; the icteric index was 6.1. The red blood cells numbered 4,740,000; hemoglobin 80 per cent; white blood count, 8,500; polymorphonuclears 88 per cent; lymphocytes 12 per cent; basophiles 4 per cent. The following is the blood chemistry report: Creatinin—0.9 per cent; urea nitrogen—11; sugar 105; chloride 605; protein 7.95–6.93; fibrinogen 0.57–0.31; albumin 4.34–3.74; globulin 3.06–2.90.

X-ray studies by our surgical and x-ray residents were made by injection of barium through the Miller-Abbott tube which made possible the visualization of the entire intestinal canal from the jejunum to the sigmoid and showed no obstruction or intrinsic pathological condition. The flat x-ray plate was negative; there was no evidence of intestinal obstruction or radio-opaque calculi.

The impression was: (1) Acute cholelithiasis and cholecystitis; (2) possible malignancy of hepatic flexure of colon and (3) partial intestinal obstruction.

Conservative treatment was instituted as follows: passage of Miller-Abbott tube, high enemas, intravenous fluids and blood transfusions continued until May 19, 1941. On that date there was sudden dyspnea, cyanosis with a rapid irregular pulse. Inspiratory crow was present. No evidence of pulmonary changes was found to account for the dyspnea. Laryngoscopy was performed showing definite edema of the cords. The patient was first intubated and then an emergency tracheotomy was performed. Her general condition improved and the patient

was receiving supportive treatment when she became toxic and died on May 22, 1941.

*Postmortem Findings.* There was generalized moderate atheromatosis, and slight congestion in the lower lobes and congestion of bronchial mucosa. The gallbladder was normal in size but filled to capacity by a large number of faceted, dark-green brown stones. The liver showed cloudy swelling. The kidney was congested but was otherwise normal. The thyroid weighed 200 Gm. and was markedly enlarged and nodular. One section of the thyroid was composed of cystic adenomas. There was extensive hemorrhage into the adenomas of the left lobe so that practically the whole lobe was infiltrated with blood. In the posterior portion of both lobes there was a large amount of bone formation as evidenced by brittly resistance meeting the knife as the organ was sectioned.

There was edema of the pillars of the larynx. The vocal cords appeared normal and the larynx showed a small amount of congestion. However, just below the vocal cords there were several small areas of mucosa covered by fibrin. The mucosa of the trachea became progressively more hyperemic and inflamed as one progressed toward the bifurcation at which point the inflammatory process was quite severe. The third, fourth and fifth tracheal cartilages were sectioned in their midportion. The mucosa of the trachea surrounding the tracheotomy wound was intensely congested and there was a small amount of purulent material covering the area. Further down the trachea, there were also several rather extensive areas covered by fibrin and some purulent exudate.

The presence of an extensive hemorrhage in the adenoma of the left lobe of the thyroid and the edema of the pillars of the larynx were noteworthy findings in view of the absence of a competent cause for these findings except the trauma of the tube. The extensive hemorrhage into the adenoma of the left lobe of the thyroid we believed was due to surgical procedure employed to reach the trachea. A spontaneous hemorrhage into the adenoma before the tracheotomy was performed was possible, but although spontaneous hemorrhages do occur, they are seldom of such severity as

to require tracheotomy (Hertzler,<sup>12</sup> Boyd,<sup>8</sup> Crotti<sup>10</sup>). Spontaneous hemorrhage is more common in the fetal adenomas (Hertzler)<sup>12</sup> but there is little doubt that very many of the nodular adenomas commonly regarded as fetal in type are essentially the same character as colloid adenomas. According to Boyd:<sup>8</sup> "It appears that it is a mistake to draw any fundamental distinction between the colloid and fetal types of adenoma." These hemorrhages are of pathological rather than surgical interest. W. C. McCarthy<sup>16</sup> has never seen a hemorrhage into a fetal adenoma extensive enough to necessitate an emergency surgical intervention. A. Graham<sup>11</sup> believes that in the majority of cases hemorrhage into the fetal adenomas is of no clinical significance. G. W. Crile,<sup>9</sup> in a clinical analysis of 20,000 thyroid operations makes no mention of hemorrhage into fetal adenomas as the primary reason for operative interference.

The second important anatomopathological finding is the edema of the larynx. Acute edematous laryngitis rarely occurs as a primary affection but is secondary to septic tonsillitis, pharyngeal phlegm, peritonsillar abscess, erysipelas, or Ludwig's angina. None of these was present in our case. We can also exclude any systemic affection, as specific fevers, diabetes, Bright's disease or alcoholism as contributing factors.

Prolonged intubation with suction can produce irritation of the nasopharynx (Johnston,<sup>15</sup> Wangensteen<sup>19</sup>). Indirectly also the tube may contribute to this edema, by allowing regurgitation of the acid stomach contents, and this by chemical action, together with traumatic effect of the tube, produce such acute dramatic respiratory embarrassment as to require tracheotomy. Examination of the larynx by Guedel Foregger laryngoscope was done before resorting to tracheotomy and demonstrated marked edema of the arytenoids with obliteration of the interarytenoid fossa.

## CONCLUSION

Review of the literature reveals reports of nine cases of severe laryngeal injury requiring tracheotomy produced by inlying suction tubes. To these we add one case of acute edema of the larynx requiring tracheotomy produced by intubation with a Miller-Abbott tube.

We believe that careful daily inspection of the larynx should be performed in all patients requiring prolonged intubation with inlying suction tubes.

Edema may result not only from the trauma of the tube but also by reason of regurgitation of the acid stomach contents. In our case the degree of edema required immediate tracheotomy for control of asphyxia. Its sudden onset and intensity of obstruction would not seem to have been the result of the chronic long-lasting thyroid enlargement.

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# ENTEROCYSTOMA WITH TWISTED PEDICLE

J. MURRAY BEARDSLEY, M.D.

Associate Surgeon, Rhode Island Hospital

PROVIDENCE, RHODE ISLAND

THE occurrence of enterocystoma has been noted by several authors although it is among the more uncommon of the mesenteric cysts. It may occur in any portion of the alimentary tract with the terminal ilium being the most common site.

In the past much discussion has been centered around its mode of origin but it is now generally agreed that incomplete involution of the omphalomesenteric duct is the true explanation of this type of cyst.

The following case is reported first, because of the rarity of the condition and second, it is of interest because the cyst had a well developed pedicle around which it had become twisted, giving rise to abdominal symptoms and signs suggestive of acute appendicitis. In this instance the pedicle arose from the mesenteric border of the bowel in contrast to the more common site on the antimesenteric surface.

## CASE REPORT

M. D., an eight-year old, white female was admitted to the Rhode Island Hospital on June 29, 1940 with the chief complaint of pain in the right lower quadrant. The patient had been well until the morning of admission when she noted cramp-like pain of moderate severity in the midabdomen. This had persisted intermittently, becoming somewhat worse in the evening when the pain localized in the right lower quadrant. Relief from pain was obtained by keeping the legs flexed upon the abdomen. She had been nauseated but denied vomiting. Her bowels had moved normally the day previous to admission. There had been no urinary symptoms. Her past history was irrelevant.

Physical examination revealed a well developed and well nourished eight year old girl, alert and co-operative. She appeared moderately ill and apprehensive. Apart from hypertrophied tonsils general physical examination

was not remarkable except for the abdomen. The abdomen exhibited spasm on the right side with localized tenderness at McBurney's point. Rebound tenderness was referred to the same region; no masses were noted on palpation. The white blood count was 18,400 with 96 per cent polymorphonuclear neutrophiles. Urine examination was negative except for an occasional white blood cell. Her temperature was 99.0°F., pulse 124 and respirations 24.

The diagnosis of acute appendicitis was made and the patient was taken to the operating room shortly after admission. (Fig. 1.)

The abdomen was opened through a right rectus, muscle splitting incision. A moderate amount of serous fluid was present in the peritoneal cavity. The appendix was delivered without difficulty and showed some evidence of peri-appendiceal inflammation but otherwise appeared normal. It was removed in the usual manner and the stump was carbolized and buried. The terminal ilium was explored and a tumor was encountered 6 inches from the ileocecal valve. It was of elastic consistency with a smooth surface and not adherent at any point. It was attached to the mesenteric surface of the ilium by a pedicle which was 1 cm. in diameter but widened out to 2 cm. at its attachment to the tumor. The tumor mass was estimated to be 4 cm. in diameter and was twisted on its pedicle with one complete turn. The blood supply did not appear to be completely occluded and there was no evidence of gangrene or necrosis although the tumor had a cyanotic appearance. Improvement in circulation was noted as soon as the torsion was relieved. The tumor was removed after transfixation of the pedicle. The wound was then closed in the usual manner. The postoperative course was uneventful. Culture of the fluid from the peritoneal cavity showed no growth of organisms.

*Pathological Report.* (Dr. Robert J. Williams.) "Gross Description: Specimen consists of a spherical cystic structure measuring four centimeters in diameter. It is filled with a thin cloudy fluid. The external surface, to which is attached a delicate pedicle, is gray, smooth and

glistening. The wall of the cyst is one to three millimeters in thickness and its inner surface is rough and ragged. (Fig. 2.)

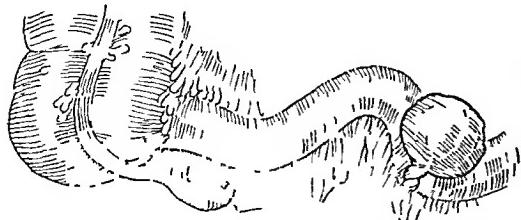


FIG. 1. Enteric cyst of terminal ileum twisted upon its pedicle.

**"Microscopical Description:** The cyst wall is composed of a well developed mucosa with a muscularis mucosa, sub-mucosa, a muscular coat composed of two layers of smooth muscle and a scrosa.

"The mucosa is lined by a single layer of tall columnar epithelium with a cuticle-like border. Simple glands, opening by a short duct directly on the surface, are scattered irregularly throughout the mucosa. These glands are lined by a layer of epithelial cells similar to those on the surface. Occasional goblet cells are present. Lymphocytes and eosinophilic leukocytes are scattered through the mucosal stroma. The muscularis mucosa is absent in places. The

smooth muscle fibres in the two layers of the muscular coat course at right angles to each other.

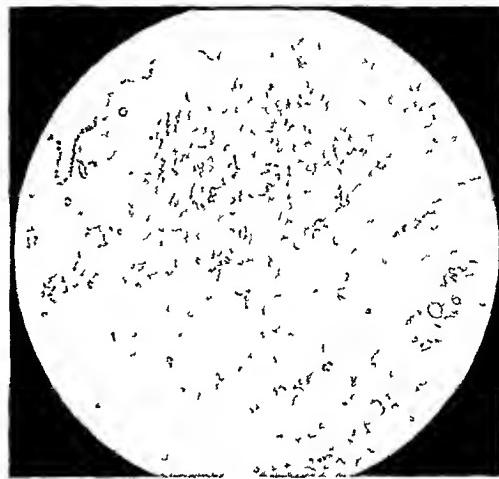


FIG. 2 Photomicrograph of cyst wall.

"In places there is ulceration of the mucosa and infiltration of all layers by an exudate of polymorphonuclear leukocytes, fibrin, erythrocytes and a few lymphocytes and large mononuclear cells.

**"Diagnosis:** Enterocystoma of ileum with acute inflammation."

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# RICHTER'S HERNIA\*

## CASE REPORT

EDWARD VERNON MASTIN, M.D.

Assistant Professor of Surgery, St. Louis University School of Medicine

ST. LOUIS, MISSOURI

THE following is a case report of Richter's hernia successfully handled:

### CASE REPORT

A man, forty-five years of age, was admitted to the hospital with a history of pain and a tender mass in the right subinguinal region, which had been present for three days. He also complained of nausea and vomiting and inability to move his bowels during the last twenty-four hours. Examination showed a tender mass protruding from the right fossa ovalis. His temperature was 101.6° F., the pulse was 112 and his white blood count was 17,000. There was moderate abdominal distention. A diagnosis of strangulated femoral hernia was made, and immediate operation advised.

An incision was made below the inguinal ligament and the femoral sac was identified. The sac was definitely bluish red in color and upon opening it a half ounce of bloody fluid escaped. A portion of a loop of small intestine was seen protruding through the femoral canal. This was markedly swollen and definitely gangrenous. It was believed that the hernia could not possibly be reduced without rupture of the gangrenous area with associated contamination of the peritoneal cavity, so the only safe procedure was to establish an ileostomy by simple incision in the bowel through the gangrenous area and thus relieve the obstruction. The wound edges were protected by vaseline gauze and a small rubber tube was then placed in the lumen of the ileum.

The patient gradually improved and after two weeks the edges of the bowel appeared healthy and the wound was beginning to granulate. The patient was then given sulfanilaguanidine in doses of 15 gr., five times a day for one week prior to closing the ileostomy. A right rectus incision was made and the ab-

dominal viscera adequately walled off and the loops of ileum proximal and distal to the ileostomy were identified. Two rubber-covered intestinal clamps were placed on each loop of the bowel about eight inches from the ileostomy opening. Then a small irrigating catheter was passed through the ileostomy wound by an assistant and each loop of bowel was thoroughly irrigated with a solution of sulfanilaguanidine. When it was believed that these loops were reasonably clean, all excess fluid was expressed and several abdominal pads were placed under the loop of ileum and the bowel was carefully separated from its attachment in the femoral canal. The edges of the opening in the ileum were then freshened and the opening closed transversely by two rows of sutures of chromic catgut, which were reinforced with several interrupted sutures of silk. The bowel was then cleansed with saline and replaced in the abdomen.

The attachment of the bowel in the femoral canal was cleansed and the peritoneum surrounding it was excised. Then this opening in the peritoneum was closed with chromic catgut. The abdomen was closed in a routine manner. A rubber drain was placed in the opening in the femoral canal and about a week later a secondary closure of the femoral canal was made.

### COMMENT

The method described is a safe one for the treatment of a strangulated femoral hernia, as there is little or no risk connected with the operation. Too often when one attempts a primary resection of gangrenous bowel, when there is marked distention, due both to fluid or gas, the sutures do not hold and there will be a leak with resulting peritonitis.

\* From the Department of Surgery, School of Medicine of the St. Louis University, St. Louis, Missouri.

# EFFECT OF PREGNENINOLONE (ETHINYLY TESTOSTERONE) UPON HUMAN CERVICAL SECRETION\*

CHARLES H. BIRNBERG, M.D.,

Chief of the Department of Female Sex Endocrinology,  
and Associate Obstetrician, Jewish Hospital

LAWRENCE KURZROK, M.D.

Associate Obstetrician and Gynecologist, Greenpoint  
Hospital; Assistant Obstetrician and  
Endocrinologist, Jewish Hospital

AND

HENRY WEBER, M.D.

Assistant Obstetrician and Endocrinologist, Jewish Hospital

BROOKLYN, NEW YORK

IT has long been known that the cervical mucus is normally alkaline, and that penetration of sperm through the cervical secretion is apparently much better when this condition prevails than when the hydrogen ion concentration tends to be more acid. Efforts up until this time to change the acidity of cervical mucus from a hydrogen ion concentration of 5 to 6 to that of an alkaline hydrogen ion concentration of 8 have not met with much success. An acid cervical mucus is a deterrent to semen penetration and thus can cause sterility.

During the course of investigation of a group of women complaining of sterility, six cases were encountered in whom the semen penetration test<sup>1</sup> was negative. This test consists of putting a drop of semen and cervical mucus upon a slide, so that the surfaces become contiguous when covered by a glass cover slip. The test is positive if columns of spermatozoa can be seen (under the microscope) in the cervical mucus. The test is negative when the spermatozoa are repelled by the mucus so that they cannot penetrate it. At the same time that this test was performed, the hydrogen ion concentration of the cervical mucus was determined. An indicator with a range from a hydrogen ion concentration of 4 to 10 was used. In five of these cases the hydrogen ion concentration was 6 or less during various phases of a menstrual cycle. There was no local condition such

as endocervicitis which might possibly account for this abnormality. Attempts to alter this condition by local treatment, injection of estrone or progesterone failed. Repeated attempts at artificial insemination were also unsuccessful. These patients were then given 10 mg. of pregneninolone (pranone) twice a day through the cycle and the effects observed. The case reports follow:

## CASE REPORTS

CASE I. G. M., age thirty, married four years, had never been pregnant. General physical and vaginal examinations were negative (except for a slight degree of cervical hypoplasia). Basal metabolism was +10. Endometrial biopsy showed a mixed endometrium with secretory changes. Lipiodol revealed a normal uterus with patent tubes. Weekly vaginal smears ranged from +3 to +4, vaginal hydrogen ion concentration from 4 to 6. Semen penetration was negative. The hydrogen ion concentration of the cervical mucus was 6. Nine attempts at artificial insemination were unsuccessful. Five mg. of proluon given in the second half of the cycle every other day did not alter either the cervical hydrogen ion concentration or the penetration test. This procedure was carried out for three successive months. Ten mg. of pregneninolone (pranone) tablets were given twice a day and after six weeks the hydrogen ion concentration was 8 and penetration test was positive. Three weeks later the patient became pregnant.

CASE II. I. B., age twenty-eight, sterile for four years had a normal menstrual history.

\* From the Division of Female Sex Endocrinology, Brooklyn Jewish Hospital.

General examination was negative except for a slight hypoplasia of the cervix. Basal metabolism was -10. Lipiodol revealed a normal uterus and patent tubes. The hydrogen ion concentration of the cervical mucus was 5. Semen penetration test was negative. The patient had received therapy for five months, including biweekly injections of pregnancy urine gonadotrophic extract (Antuitrin-S), bi-weekly injections of 10,000 International Units of an estrogen, subsequently followed by

then occurred every twenty-eight days until the present time. There was no dysmenorrhea or other menstrual molemina. Hormone study revealed a negative prolan and 9 rat units of estrone. Premenstrual endometrial biopsy revealed secretory changes in the endometrium. Weekly vaginal hydrogen ion concentration ranged from 4 to 5, vaginal smears from -3 to +4. The hydrogen ion concentration of the cervical mucus was 6 and the semen penetration test was negative. Injection of 5 mg. of

TABLE I

Patient	Age	Endometrial Biopsy	Cervical Hydrogen Ion Concentration through Cycle	Semen Penetration through Cycle	Pregneninolone (Ethinyl Testosterone) Dose	Results—Cervical Hydrogen Ion Concentration
1. G. M. Para I.	30	Proliferative with some secretory changes	6 6 5	Negative “ “	10 mg. twice a day, 6 weeks	Hydrogen ion concentration 8 after six weeks
2. I. B. Para I.	28	None	6 6 5	“ “ “	10 mg. twice a day, 7 weeks	Semen penetration positive Pregnancy in three weeks Hydrogen Ion Concentration 7 after seven weeks
3. F. S. Para I.	26	Secretory	6 6 6 6	“ “ “ “	10 mg. twice a day, 7 weeks	Semen penetration positive Pregnancy three weeks later Hydrogen Ion concentration 8 in seven weeks
4. E. M. Para II.	30	None	6 5 5 5	“ “ “ “	10 mg. twice a day, 8 weeks	No pregnancy Hydrogen ion concentration 8 in eight weeks
5. A. H. Para I.	32	Secretory	5 5 5	“ “ “	10 mg. twice a day, 10 weeks	Semen penetration positive Pregnancy two weeks later Hydrogen ion concentration 5
6. D. M. Para I.	25	None	5 8 8 8	“ “ “ “	1. 5 mg. twice a day, for 4 weeks 2. 10 mg. twice a day, for 4 weeks	Semen penetration unchanged No pregnancy No change Semen penetration positive in six weeks No pregnancy

injection of progesterone, previous to her present study. Weekly vaginal smears and vaginal hydrogen ion concentration were normal. Ten mg. pregneninolone (pranone) tablets twice daily were prescribed for her. After seven weeks the semen penetration test was positive and the cervical hydrogen ion concentration was 7. After ten weeks the patient became pregnant.

CASE III. F. S., age twenty-six, had been sterile six years. Her menses began at fifteen, were irregular for about seventeen months, but

progesterone every other day in the second half of the cycle (for two successive periods) also did not bring any change. Administration of 10 mg. pregneninolone (pranone) tablets twice a day throughout the cycle brought about a positive semen penetration test and a cervical hydrogen ion concentration of 8 in seven weeks. The patient, however, has still not become pregnant.

CASE IV. E. M., age thirty, has one child five years old but has been unable to become pregnant for the past three years. General

examination was entirely negative. Basal metabolism was +4. Hormone study (pre-menstrual) revealed a negative prolan and 12 rat units of estrone. Weekly vaginal smears and hydrogen ion concentration were normal. The hydrogen ion concentration of the cervical mucus was 5 to 6. The semen penetration test was negative. The patient was given 10 mg. of pregneninolone (pranone) tablets twice a day and after eight weeks the hydrogen ion concentration was 8. The semen penetration test was positive and the patient became pregnant two weeks later.

CASE V. A. H., age thirty-two, had been sterile seven years. In 1933, she had a spontaneous miscarriage at five months followed by a dilatation and curettage. Menses began at sixteen; it occurred every twenty-eight days and lasted six days. The patient's breasts were painful for about one week premenstrually. Basal metabolism was +8. X-ray of the uterus revealed bilateral patency of tubes. Premenstrual endometrial biopsy revealed secretory changes in the endometrium. Weekly vaginal hydrogen ion concentrations and smears were normal. The hydrogen ion concentration of the cervical mucus was 5 and the semen penetration test was negative. The patient was given 10 mg. of pregneninolone (pranone) tablets twice a day for ten weeks. However, no change in cervical hydrogen ion concentration of semen penetration test has been observed up to the present time.

CASE VI. A twenty-five-year old married woman, complained of secondary sterility. Three years before, immediately after marriage, an abortion had been performed. The physical examination was essentially negative. Menses were regular, monthly, and associated with dysmenorrhea. The basal metabolism was -2. The Rubin test was positive. Vaginal smears showed cornified epithelium. Prolan was negative, estrone was 6 rat units in a twenty-four-hour specimen. She had been treated with corpus luteum and pregnant mare serum every other day for one month with no results. She was first seen on February 9, 1941. The hydrogen ion concentration of the cervix was 8 and a

semen penetration test was negative. The semen examined at this time showed a normal morphology and the total quantity was 5 cc. Viscosity was slightly below normal and the total number of spermatozoa was 35,000,000. She was given pregneninolone (pranone), 5 mg. tablets twice daily. Her last menstrual period was on February 2, 1941. On February 21, 1941 another semen penetration test was done. It was still negative although a number of spermatozoa penetrated the cervical secretion. She menstruated again on March 4, 1941. Pregneninolone (pranone) tablets were increased to 20 mg. daily. On March 19, 1941, a semen penetration test was done and this time quite a large number of spermatozoa penetrated the cervical mucus. These spermatozoa, however, shortly lost all motility. The semen examined at this time showed no change from the previous examination. On March 31, 1941, another semen penetration test was done and at this time the test was normal. The patient menstruated again on April 6, 1941.

#### SUMMARY

1. Pregneninolone (pranone) was given to six patients who had a negative semen penetration test and a hydrogen ion concentration of cervical mucus ranging from 5 to 6; the hydrogen ion concentration in one of the cases, however, was 8.
2. The acidity of the cervical mucus was changed to a hydrogen ion concentration of 7 or 8 and semen penetration test became positive in five cases.
3. Three of these patients subsequently became pregnant.
4. There was no change in one case.

We wish to thank the Schering Corporation for their generous supply of Ethinyl Testosterone (Pranone).

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# ADVANTAGES OF EARLY OPERATION IN UNDESCENDED TESTIS

L. M. RANKIN, M.D.

Chief of Service, Delaware County Hospital

AND

SHERMAN A. EGER, M.D.

Assistant Surgeon, Delaware County Hospital

UPPER DARBY, PENNSYLVANIA

IT is definitely known that the longer a testicle remains undescended, that is outside of its normal position in the scrotum, the greater are the possibilities of permanent impairment of its physiological functions. Furthermore, an undescended testicle is more liable to torsion, trauma, inflammation and malignancy.

With the knowledge of these dangers and with the introduction of hormonal therapy and improved surgical technic, the practice of waiting for spontaneous descent of undescended testicles at puberty is rapidly being discontinued. One would expect a deficiency in hormones to be more of a causative factor in bilateral undescended testicles than in unilateral cases and that the latter would be less responsive to hormonal therapy. This was proved by Einhorn and Rowntree<sup>1</sup> who in a study of forty cases of cryptorchidism treated by hormones, found that complete descent occurred in 43 per cent of bilateral and only 23 per cent of unilateral cases. It is, therefore, evident that the failure of the descent of the testis is due to mechanical factors in the majority of cases and especially in the unilateral ones. Furthermore, Mimpriss<sup>2</sup> found a co-existing hernia in 85 per cent of 137 patients operated upon. Strauss<sup>3</sup> in a series of thirty-eight cases found hernias in 82 per cent and stated that in these the descent of the testicle or cure by injection therapy could not be expected.

In the past three years we have operated on seven patients with undescended testes at the Delaware County Hospital in Drexel Hill using the two-stage method described by Torek<sup>4</sup> and known as the Torek operation. Five of these cases have been completed surgically and are here-with reported. Two more recent cases have

only had the first stage completed and will not be included. Although this series is comparatively small, it has presented certain factors worthy of note.

## CASE REPORTS

CASE I. J. B., age five, had his left testicle in the normal position in the scrotum. At operation the right testicle was high in the inguinal canal near the internal ring, slightly smaller than normal and was accompanied by a hernia. Sufficient cord length was obtained to permit anchoring of testicle to the thigh without tension; the hernia was repaired. The second-stage operation was performed four months later. After three years the right testicle was the same size as the left, it was freely movable and in the normal position in the scrotum.

CASE II. M. B., age twelve. The right testicle had always been normal in the scrotum. During two years of hormonal therapy, starting at age ten, the left testicle descended from the midinguinal region into the perineum lateral to the scrotum. At operation the left testicle was slightly smaller than the right and was accompanied by a hernia. Sufficient cord length was obtained to permit anchoring testicle to the thigh without tension and the hernia was repaired. The second-stage operation was done four months later. After three years the left testicle was one-third smaller than the right, it was freely movable and in the normal position in the scrotum.

CASE III. J. B. age thirteen. The patient's left testicle had always been normal in the scrotum. Hormonal therapy had been carried out for two years, starting at the age of eleven for tender, undescended right testicle without benefit. At operation the right testicle was definitely smaller than the left in the midinguinal canal and was accompanied by a hernia. The shortened vas necessitated higher anchorage of the testicle to the thigh than desirable. The hernia was repaired. The second-

stage operation was performed four months later. After three years the right testicle was one-half the size of the left, freely movable, but higher in the scrotum.

CASE IV. J. B., age thirteen. The patient's right testicle had always been normal in the scrotum. No hormone therapy had been used. At the age of three it was discovered that the left testicle was undescended. The physician advised the parents to wait until puberty for operation. At operation the left testicle was smaller than the right and was in the midinguinal canal, accompanied by a hernia. The shortened vas necessitated higher anchorage of the testicle to the thigh than desirable and the hernia was repaired. A second-stage operation was done five months later. After six months the left testicle was one-half the size of the right and freely movable in the midsrotal position.

CASE V. R. U., age ten. A right undescended testicle was discovered at the age of two and the physician advised waiting until the age of ten for operation. No hormonal therapy was carried out. The left testicle was normal in size and was located high in the scrotum and would retract to the midinguinal canal. At operation the right testicle was very small in the midinguinal canal and was accompanied by a hernia. The shortened vas necessitated higher anchorage of the testicle to the thigh than desirable and the hernia was repaired. The left testicle was normal size in the inguinal canal near the external ring and was accompanied by a hernia. Sufficient cord length was obtained for anchorage of the testicle to the thigh without tension and the hernia was repaired. A second-stage operation was performed four months later. After six months the right testicle was still very small, freely movable and in the midsrotal position. The left testicle was normal in size, freely movable and normal in the scrotum.

#### SUMMARY

1. Case I, II and III were brothers.
2. The best result was obtained in Case I in which the undescended testicle was

found to be normal in size at operation and the vas not shortened.

3. Less satisfactory results were obtained in the remaining four patients, ranging in age from ten to thirteen years, in all of which the undescended testicles were found to be smaller than normal at operation and have not increased in size since.

4. In the older patients the vas was relatively short, preventing the testicle from being placed in an ideal position in the scrotum.

5. A hernia accompanied each undescended testicle in this series.

#### CONCLUSIONS

The high percentage of mechanical factors causing incomplete descent of the testicle, as well as the high incidence of associated hernia, makes operation the treatment of choice in the vast majority of cases. We believe that the best age for operation is around five years, because by that time the child is properly trained in toilet habits, thus minimizing the chances of contaminating the operative wounds; after that age the degree of testicular atrophy and relative shortening of the vas increases, thereby influencing, proportionately, the physiological and anatomical results.

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# New Instruments

## A NEW INSTRUMENT FOR FACILITATING THE ADMINISTRATION OF INTRAVENOUS FLUID

LOWELL L. EDDY, M.D.

Surgical Resident, Virginia Mason Hospital

SEATTLE, WASHINGTON

ONE of the technical problems encountered in administering intravenous fluids at the antecubital fossa, the usual infusion site, is that the patient's arm and forearm commonly must be immobilized at the elbow during the procedure. The associated pain and resulting stiffness are a source of considerable discomfort, which this new instrument practically eliminates. Infusions in the forearm and wrist do not require immobilization of the elbow but in many patients the antecubital veins are better suited anatomically for intravenous procedures.

We are presenting an instrument that fixes the intravenous needle in a vein at the antecubital fossa and still allows moderate freedom of motion at this joint during an infusion. Many "needle-holders" have been devised to immobilize a needle in a vein, i.e., to prevent anteroposterior and lateral motion. To our knowledge there has been no device described that has the characteristic features of the instrument here presented. (Fig. 1.)

During a clinical trial with more than 1,000 infusions using this intravenous clamp at The Brooklyn Hospital and The Lenox Hill Hospital in New York and The Virginia Mason Hospital in Seattle it has been found unnecessary to immobilize the upper extremity even during prolonged intravenous procedures.

If the patient flexes his arm more than

ninety degrees, the proximal end of the clamp will press against the upper arm, breaking any further upward movement.

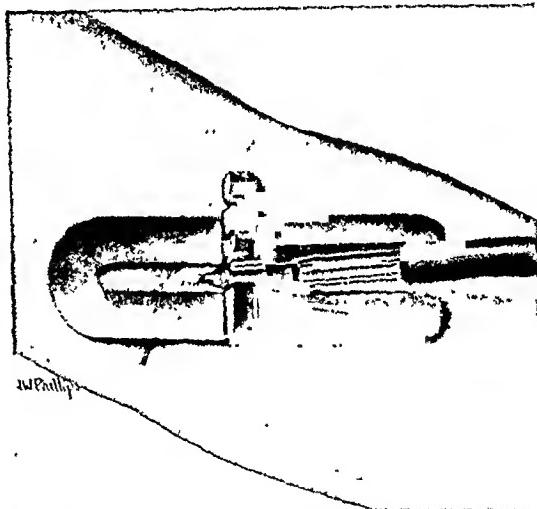


FIG. 1. Sketch of the intravenous clamp in position. Note oblique direction of the needle.

But the flow of the infusion is not obstructed, for when the elbow is flexed the proximal end of the clamp rolls the mobile soft tissues and the vein with its needle medialward in an oblique direction rather than compressing the vein wall.

The actual application of the intravenous clamp to a needle with a rectangular hub is illustrated in the accompanying pictures. Insert the needle to its hub after entering the skin about one inch distal to the flexion crease at the elbow. Advance the open end of the U-shaped clamp from above downward along the skin over the shaft of the

needle until the vise portion of the clamp is at the needle hub. (Fig. 2.)

Tilt the glass connecting tube to a ten

vein. With the instrument in this position about ninety degrees of motion of the elbow joint is permitted. (Fig. 4.)



FIG. 2. Method of applying the instrument. Advance the intravenous clamp from above downward to the needle hub.



FIG. 3. Final position of the instrument. Note the placement of the adhesive tape.

degree angle above the metal base of the clamp; then tighten the screw to the vise. Next, strap each end of the clamp firmly

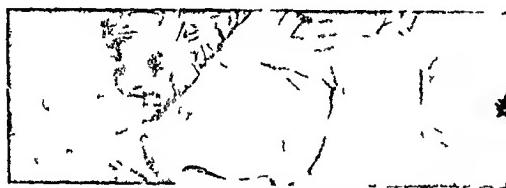


FIG. 4. An illustration of a patient reading a paper during an infusion.

to the arm with adhesive tape, the upper strap above the bend of the elbow, holding the instrument over the antecubital fossa as in Figure 3.

The open slit of the U-shaped clamp should overlie the oblique course of the

A new instrument called an intravenous clamp is presented. It is a needle holder with the characteristic feature that it fixes a needle in one of the veins at the antecubital fossa and still allows moderately free motion of the elbow joint during an infusion, thus eliminating the use of the arm board. Its value is best demonstrated during prolonged intravenous procedures and with nonco-operative patients who resist restraint.

The use of this instrument to facilitate the administration of plasma to the war wounded enroute from battle field to hospital is suggested.

I acknowledge with appreciation the efforts of Mr. Waldemeyer Ayers for his part in the design and creation of this instrument.



# A COMMON DUCT FORCEPS AND A FLEXIBLE CANNULA\*

R. RUSSELL BEST, M.D.  
OMAHA, NEBRASKA

DURING the last ten years, opening and exploring the common duct has become a more and more frequent

most frequently used. This is particularly true in the obese individual, in cases in which the common duct is very deep within

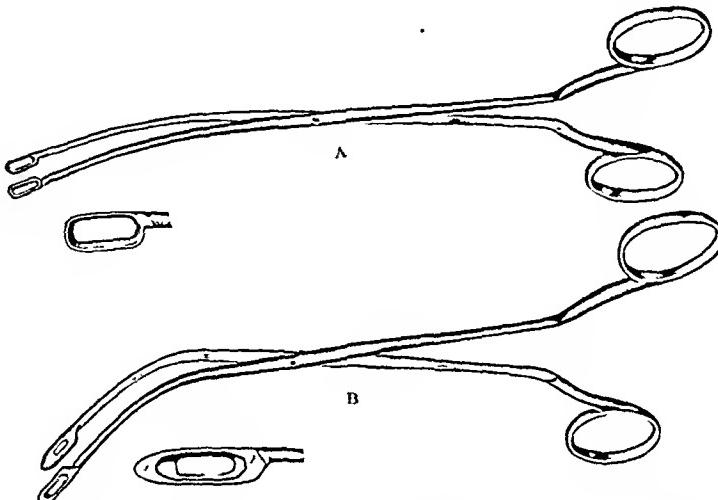


FIG. 1. A, shows instrument with insufficient curve. B, shows the recently designed instrument with the end which serves as a dilator.

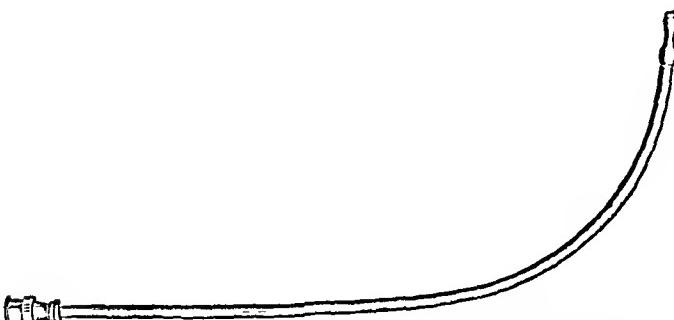


FIG. 2. A flexible silver cannula with beaded area for dilatation of sphincter area. A Luer syringe may be attached to the other end for irrigating purposes.

accompaniment of cholecystectomy. In my own series, it has been carried out in about 30 per cent of the cases. A thorough exploration of the common duct requires palpation for stones, and visualization for thickening or dilatation of the duct, followed by internal exploration by means of forceps, scoops, irrigations and suction. Many times one is handicapped in getting into the common duct with the duct forceps

the abdomen, or when the surface of the common duct, which can be exposed between the upper margin of the duodenum and undersurface of the liver, is very short.

The usual common duct stone forceps has the angle shown in Figure 1 A. There is a modification of this instrument with a slight, but not sufficient, increase in the curve and with only a very short curved portion so that one cannot get far down

\* From the Department of Surgery, University of Nebraska College of Medicine.

into the common duct. Figure 1 B depicts a recently designed instrument that I have been using in which the degree of curve is greater, and in working at a depth one has no difficulty in maneuvering the instrument into the common duct. Also because the instrument is longer beyond the lock, one can easily reach the lower confines of the common duct. The head of this common duct stone forceps is shaped so as not only to be able to grasp stones but the bulbous tip also permits the instrument to pass through the sphincter area and act as a dilator. I do not believe it is necessary to open the forceps and dilate the sphincter area further.

Exploration of the common duct is not complete until the duct has been irrigated with sterile normal saline and certainly one

is not sure that the lower end of the duct is freely open until it has been definitely established that fluid can be irrigated directly into the duodenum. With a rubber catheter this has always seemed a rather awkward and cumbersome procedure, sometimes consuming considerable time. The flexible silver cannula shown in Figure 2, which is rather similar to a Mixter cannula, may be angulated so as to be easily inserted into the common duct and directly through the sphincter area without difficulty, if no obstructing agent is present. The end is blunt and beaded and the larger olive-shaped area just behind this enables one to use the instrument as a small caliber dilator and probe. At the proximal end there is a hub for attachment of a Luer syringe.



IN rare instances, there occurs an extreme type of sinus arrhythmia in which there is sufficient inhibition of the node to cause the heart to pause for an abnormally long period (cardiac standstill). In severe cases symptoms similar to the Adams-Stokes syndrome in heart block occur.

# THE USE OF CURVED SPIRIT LEVELS IN ORTHOPEDICS

TOUFICK NICOLA, M.D.

Clinical Professor of Orthopedic Surgery, New York Polyclinic Hospital Post-Graduate Medical School  
MONTCLAIR, NEW JERSEY

THE author has found two curved spirit levels useful in certain orthopedic procedures. The larger curved

internal rotation are read where the bubble comes to a standstill. (Fig. 3.)

2. To measure the degree of torsion of the

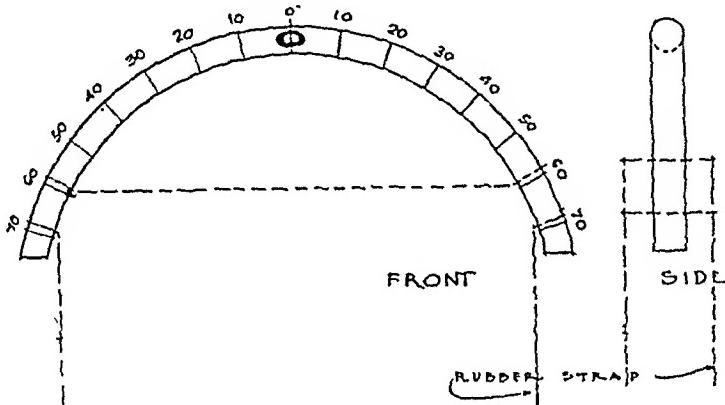


FIG. 1. Large spirit level.

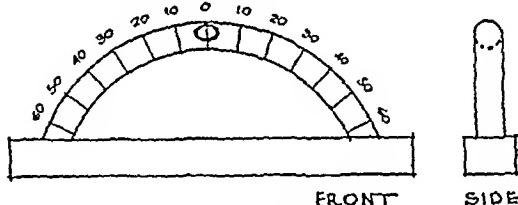


FIG. 2. Small spirit level.

spirit level (Fig. 1) has a diameter of six inches and is attached to a rubber strap two inches wide and eighteen inches long. The smaller curved spirit level (Fig. 2) has a diameter of four inches and is attached to an aluminum base. Both levels have ten degree markings.

These curved spirit levels have been found useful:

1. To measure degrees of rotation in the hip joint. To do this the large curved spirit level is strapped to the lower thigh just above the knee with the zero mark in line with the center of the patella (marked with a skin pencil). When the limb is rolled in, then out, the degrees of internal and ex-

tibia. Two curved spirit levels are used in this determination. The larger one is strapped to the lower thigh as described above. The smaller one is placed on the plane connecting the tips of the internal and external malleoli. The difference in the readings between the two curved spirit levels gives the degree of torsion of the tibia. (Fig. 4.)

3. To direct the Smith-Petersen nail, wire or screw in extra-articular treatment of fractured hips. A lateral x-ray is taken (Dooley) and from this x-ray the angle of torsion, between the axis of the neck of the femur and the bicondylar axis (angle of inclination), is determined. If this is twenty

degrees and if, after reduction, the thigh is rolled in twenty degrees, then the smaller spirit level (placed on the driver which

which is placed just above the patella. If the limb is rolled in thirty degrees in cases in which the angle of inclination is found to

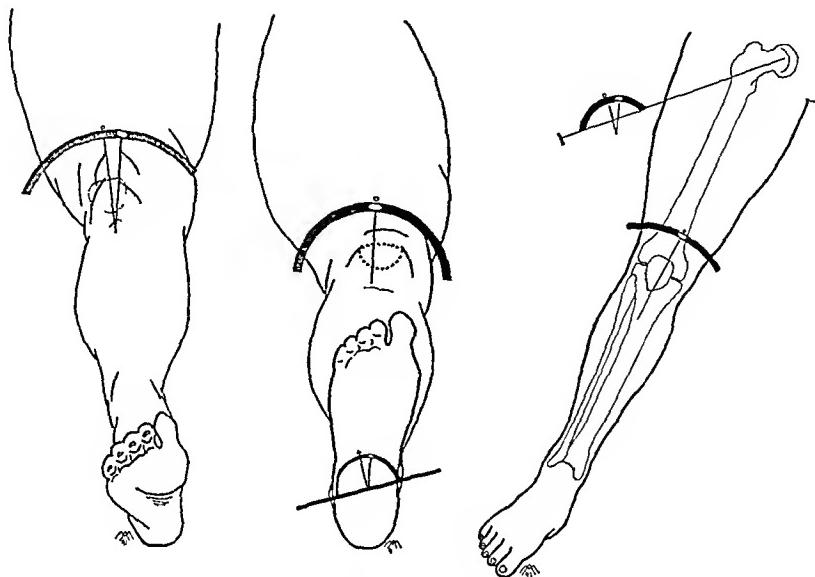


FIG. 3.

FIG. 4.

FIG. 5.

FIG. 3. Measuring degree of rotation at hip.

FIG. 4. Measuring torsion of tibia.

FIG. 5. Measuring direction of Smith-Petersen nail, wire or screw.

directs the nail, wire or screw) should read zero. The degree of internal rotation of the hip is read on the larger curved spirit level

be twenty degrees, the smaller curved spirit level should read ten degrees. (Fig. 5.)



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## Editorial

### ACUTE CONDITION OF THE GALLBLADDER

**A**N acute condition of the gallbladder may consist of a spasm of the wall, it may be a pericholecystitis or it may be the sequel of this disorder. If the organ is surrounded by adhesions of the omentum, possibly of available neighboring intestines, there may be necrosis of the wall with leakage and the formation of a neighboring abscess, or the gallbladder may be gangrenous with death of the entire organ.

The diagnosis of an acute condition of the gallbladder obviously is a very difficult problem. The spasm of the gallbladder is a very unpleasant experience as any patient who is having one will tell you. Pain in the upper right quadrant radiates to the subscapular region or some other area of the back. It is attended by much lamentation, the sound of which is more impressive than the physical phenomena. The patient may prespire but there are no symptoms of collapse and no graying of the skin. The pulse rate may be increased but the pulse is not running and thready. In the milder cases one may give the patients sedatives by mouth and a hot pack. It is possible that the pain will subside before the sedative given has time to act. If the pain is more severe, the doctor gives subdermically a quarter grain of morphine. If there is a nurse about to administer the drug, it will very likely be prescribed. At any rate the pain subsides and soon the patient is ready to do what she has in mind, albeit with some residual soreness.

If in the futile attempt to expel the offending stone the wall of the gallbladder becomes inflamed and a fibrinous exudate forms on its surface, the great omentum is attracted and by augmenting the size of the distended organ a palpable tumor is produced sensitive to the touch and accompanied by muscular rigidity. If the patient has the leisure and has the services of a nurse, this period is considerably important. Hot packs should be applied and bed rest on her back should be prescribed. The laboratory is set in motion, x-rays are made which, if done capably, will show the number and size of the stones. The condition now enters the scientific stage and the patient may be said to be having adequate medical care. On the other hand, if the patient is neither poor enough nor rich enough to command such services and has a flock of children to get off to school, she usually manages to get about for a few days until the pain subsides. She does not have adequate care because the doctor does not know the size and the number of the stones.

If the regression does not take place in a few days, one of two processes may supervene: The inflammation may subside but the obstruction to the cystic duct may remain and the gallbladder becomes distended because its contents cannot escape. We then have a hydrops of the gallbladder. This is signalized by subsidence of the muscular rigidity while a rounded tumor remains. These tumors may become very

large. I have seen one drained by an incision just above Poupart's ligament under a mistaken diagnosis by an eminent surgeon. I saw one which extended into the pelvis and was mistaken for an ovarian cyst.

On the other hand, the gallbladder remains large, the muscular rigidity continues and the tenderness increases. The patient is bedfast, and if this continues beyond four days, the possibility of involvement of the gallbladder wall comes into question. It may be seeping bile because of a local necrosis of the wall, which by flowing over the watershed of the great omentum may overshadow the original lesion and an appendiceal abscess be diagnosed. Or an abscess may form on the surface which, if the omentum be active enough, encloses it and the process remains local. It may cease to be local and the abscess escape the vigilance of the omentum and a spreading peritonitis results.

If the lesion increases after the fourth day, the surgeon can see more clearly what is going on. The process now reverts from scientific medicine and becomes the problem of the practiced surgeon. If a walled-in abscess is found, the prudent surgeon will insert a drain and quit. If there is no abscess but a necrotic gallbladder, a drainage of the organ itself is imperative, and the operator must be careful not to loosen any of the protective adhesions. The stones may be left undisturbed. If there is neither abscess nor necrosis, merely a much thickened gallbladder wall with omental adhesions, the desire to remove the offending organ is tempting in inverse proportion to the experience of the surgeon. It seems logical to remove the organ and be done with it. Ofttimes the conservative surgeon attempts to remove the gallstones, leaving the organ for a later stage. He finds the stones in the cystic duct so imbedded by the edematous wall that they cannot be removed and he reluctantly decides to remove the gallbladder. Technically, the operation by an experienced operator offers few difficulties. The cystic duct and all the region about is much thickened by edema but the surgeon is able to find his land-

marks and the operation is concluded.

Here lies the devil's most perfect handiwork. The cystic vessels share naturally the edema of the tissue in which they lie. This means that after ligation a fibrinous clot cannot form, that there is but an inert mass incapable of uniting with the vessel wall and that in about a week it loosens, goes on its way and a lung embolus develops. Such accidents are not common but it is one of the most potent causes for the surgeon to long for the day when he can retire. If one must operate in such conditions, the cystic duct is ligated near the common duct but the vessels are followed upward as far as possible before they are ligated. This gives a longer plug which, theoretically at least, should be less likely to break loose.

The most severe gallbladder affection is gangrene. It is exactly like the affection of the appendix. There is an initial very severe pain, the cry of dying tissue resulting from occlusion of the cystic artery causing total death of the entire gallbladder. This may follow any of the stages noted above. After the severe initial pain of about twelve hours it ceases. The gallbladder being dead, it causes no more pain. If adhesions have not yet formed, they will not do so now. If already formed, they will loosen.

The pain having ceased, the patient likely will say she is free from pain and that she feels quite well. The pulse rate may be normal but the pulse is jerky, even like the surgeon's. The patient is interested in the ceiling while saying she feels all right. The patient has a peculiar gray tinge; she looks as if her hemoglobin is about 40 but the laboratory reports 75 per cent or more.

Better have a look at once for in about four days the living tissue separates from the dead tissue and the entire gallbladder contents escape into the more or less free peritoneal cavity. Then it is too late. Fortunately, these disasters like pulmonary embolism are rare even in the busy surgeon's practice but even one is too many. But few surgeons know the difference between necrosis and gangrene and here is the place to learn.

ARTHUR E. HERTZLER, M.D.

# Original Articles

## THE PRECANCEROUS MOUTH LESIONS OF AVITAMINOSIS B\*

THEIR ETIOLOGY, RESPONSE TO THERAPY AND RELATIONSHIP TO  
INTRAO-ORAL CANCER

HAYES MARTIN, M.D.  
Attending Surgeon, Memorial Hospital  
NEW YORK, NEW YORK

AND

C. EVERETT KOOP, M.D.  
Pennsylvania Hospital  
PHILADELPHIA, PENNSYLVANIA

THE purpose of this report is first, to call attention to the capacity of avitaminosis B to cause irritative and precancerous lesions of the oral mucous membranes; second, to describe the nature of such dietary deficiencies and the frequency with which they occur; and third, to evaluate the significance of avitaminosis B in the etiology and in the treatment of intra-oral cancer.

We shall attempt to demonstrate that degenerative and precancerous changes in the oral mucous membranes are among the important symptoms of deficiency disease, and also that avitaminosis B is the greatest single cause of such precancerous mouth lesions. In a review of the literature we have found no reference to the rôle of avitaminosis B in the etiology of mouth cancer.

We have endeavored to substantiate statistically all opinions and conclusions here expressed, but where such proof is not obtainable, we have depended upon the circumstantial evidence drawn from the clinical observations and the cumulative experience of the staff of the Head and Neck Clinic at Memorial Hospital, where about 400 new cases† of mouth and pharyn-

geal cancer are seen annually. All patients are re-examined regularly in the observation clinic as long as they survive, so that at the present time, there are about 1,500 active cases of mouth cancer being followed in the clinic and private offices of the staff.

In order to obtain specific data regarding dietary deficiencies, three parallel series of 100 cases each (I—precancerous stomatitis, II—mouth cancer, III—normal controls) were selected at random from the clinic, as will be discussed in further detail.

### NATURE AND SIGNIFICANCE OF PRECANCEROUS LESIONS IN THE ORAL MUCOUS MEMBRANES

In most cases of intra-oral cancer, there are in addition to the primary lesions, definite degenerative changes in the oral mucous membranes which obviously have antedated the malignant growth. It has long been noted that such degenerative tissue changes are found in a majority of patients with mouth cancer, and, therefore, they are commonly referred to as *precancerous*.\*\* These degenerative and precancerous

of the nasal cavities, nasopharynx, paranasal sinuses, salivary glands, intrinsic larynx, thyroid, eye and orbit, which collectively comprise about 1,000 cases yearly.

\*\* The terms, *precancerous* and *precancer*, refer to any lesion or morbid state which commonly precedes the

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changes are clearly due to some form of mild injury, persisting for a long time, in other words, to chronic irritation.

It was formerly believed that such degenerative changes were always produced by some local irritant acting within the mouth, and it is only in recent years that the existence of an intrinsic factor has been recognized; that is to say, that these lesions can be produced by a deficiency of certain essential vitamins. Thus far, clinical evidence has indicated that in this country the main dietary cause of such precancerous lesions in the oral mucous membranes is a deficiency of the vitamin B complex. There is little to show that any other vitamin except B is an important factor in this regard.

The degenerative changes which have come to be recognized as precancerous in the oral mucous membranes are: leukoplakia, subacute or chronic inflammation, vascular injection, atrophy or hypertrophy of the papillae, erosion of the epithelium, etc. Most of these can be produced by any of the various forms of chronic irritation such as tobacco, syphilis, dental trauma or sepsis.

Although in practically all clinical reports on intra-oral cancer it is accepted as a fact that chronic irritation plays an important etiologic rôle, nevertheless, opinion is not uniform as to the most responsible form of irritant and it is often implied that a single irritant (tobacco, syphilis, dental trauma, etc.) acting independently can frequently be the sole cause of cancer. Some authors stress the importance of tobacco, others syphilis, still others, sepsis, and the classic belief, dating from the days of Hippocrates, is in the singular importance of the trauma of sharp teeth. The perspective here is too narrow. In the average case

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development of a malignant growth. It should be clearly understood that a *precancerous* lesion is not the "cause" of cancer, but rather that *precancer* is a prodromal stage or prodromal symptom which indicates that the chance of developing cancer is far greater in a given case or at a given site than in the normal. In other words, precancer and cancer have at least some etiologic factors in common.

the presence of more than one irritant can be demonstrated. Since the reactions of the oral mucosa to the various irritants are so similar, it is not always possible to determine their relative etiologic significance except by therapeutic tests.

While it is probable that in most cases the cancerigenic response of the mucous membranes is due to the combined action of several factors, nevertheless, a single form of irritant may be so pronounced in a certain instance that it can be held mainly responsible; as for example, syphilis in a patient with other demonstrable lesions of that disease and positive serological tests, but with no history of smoking and no signs of a dietary deficiency. The same can sometimes be demonstrated with avitaminosis B or with overindulgence in tobacco.

Finally, the significance of a given form of irritation can depend on its chronicity and prevalence among the population as a whole, rather than on its unique cancerigenic capacity. In this respect it is probable that the stomatitis of avitaminosis B outranks all other forms of chronic irritation.

#### THEORETICAL RÔLE OF THE VITAMIN B COMPLEX IN THE ETIOLOGY AND SYMPTOMATOLOGY OF MOUTH CANCER

At least three apparently unrelated types of clinical observations can be adduced in support of the theoretical rôle of the B complex in the etiology and symptomatology of mouth cancer: the vitamin deficiency natures of (1) cancer cachexia, (2) radiation sickness, and (3) precancerous stomatitis of obscure origin.

*Cancer Cachexia.* In the Head and Neck Clinic at Memorial Hospital, our first intimation of the rôle played by dietary deficiencies in mouth cancer came about ten years ago, when we found that our unsuccessful attempts to relieve malnutrition in patients under treatment for intra-oral cancer (especially those in the advanced stages of the disease) were often not due to an insufficient caloric intake alone but also to the nature of the diet in

other respects. We found that while malnutrition was not always relieved by a high caloric diet composed of milk, raw eggs, butter, lactose, etc., the addition to this diet of a few ounces of pureed green vegetables often brought about an immediate and steady gain in weight and an improvement in the sense of well-being. For several years we continued such a dietary régime empirically, not realizing that these beneficial effects were probably mainly due to the correction of a vitamin deficiency.

*Radiation Sickness.* Not long after Minot, Cohn et al.<sup>26</sup> demonstrated that pernicious anemia could be relieved by the administration of liver concentrates, it was discovered that the so-called "radiation sickness" (malnutrition, mental depression and asthenia) associated with fractionated radiation therapy could also be markedly relieved by the administration of liver concentrates. The value of this empiric measure was noted independently by several investigators (Dictel,<sup>8</sup> Young,<sup>41</sup> Webster<sup>38</sup>) and was widely discussed among cancer therapists.

The concept of what constitutes "radiation sickness" has undergone considerable change during the past twenty-five years. The term was originally used to designate a symptom complex consisting of headache, nausea, malaise, which followed immediately after the administration of the long (twenty minutes to one hour) x-ray treatments which were necessary with the x-ray machines available a quarter of a century ago.\* These symptoms were formerly

believed to be due to the disagreeable odor and toxic effects of the ozone generated in the electrical fields of the exposed high tension aerials.

By about 1930, the earlier causes of radiation sickness had been largely eliminated, and at this time the practice of daily fractionation in x-ray therapy was introduced and the concept of radiation sickness changed. Instead of transitory nausea and headache immediately following a treatment, there occurred a different type of disability, consisting of anorexia, progressive malnutrition, asthenia, mental depression, which came on, or at least was markedly aggravated about two or three weeks after the institution of the fractionated therapy. This symptom complex then came to be known as radiation sickness and it was found that the administration of liver extract was usually followed by a noticeable improvement. When viewed with broad perspective, it is entirely reasonable to explain the latter form of radiation sickness as an acute vitamin deficiency, brought on by progressive restriction of the diet, incident to the radiation reaction, and superimposed upon other debilitating effects of the malignant tumor, such as pain and sepsis. The same syndrome, when not so clearly associated with radiation, has long been known as "cancer cachexia." In brief, radiation sickness refers to a condition which existed previous to, and is only indirectly related to radiation therapy, although aggravated by it.

*Precancerous Stomatitis of Obscure Origin.* About 1933, C. P. Rhoads, then of the Rockefeller Institute, during the course of his investigation on the etiology of certain disorders of the oral mucous membranes,

\* The therapeutic x-ray machines available during the second decade and the early part of the third decade of this century always necessitated exposed high tension aerials in the treatment room. These high tension aerials were not insulated from the air, or "shock-proofed," as in the present day apparatus and during the operation of the machine, electrical fields were produced in the air, especially opposite all sharp points. The electrical fields or coronas were evidenced by the presence of sparks and crackling noises. Within these electrical fields the air was ionized with the formation of ozone and oxides of nitrogen. These ionization products possessed a disagreeable odor, especially pronounced at the end of a long treatment period. Many patients complained of the odor and believed that their distressing symptoms were due to this cause. Some measure of

included in his clinical material a number of patients from our clinic, with precancerous lesions of the mouth.\* He demonstrated to us that in many instances such precancerous lesions improved and sometimes disappeared completely under the administration of an adequate quantity of some crude preparation rich in the vitamin B complex. During the investigation it was shown that the most dependable source of the B complex was dried granular brewer's yeast, taken by mouth.

*Preliminary Conclusions.* The strong presumptive evidence of the observations just described lead us to begin the routine administration of vitamin B usually in the form of brewer's yeast,† to all patients under treatment for intra-oral cancer. The results of such a routine were so gratifying that although there are as yet no methods available for obtaining absolute statistical proof, we nevertheless concluded empirically that the abnormal changes in the oral mucosa resulting from avitaminosis B are

\* The concept of inflammatory, ulcerative and atrophic lesions of the oral mucous membranes as a manifestation of a dietary deficiency, dates from the early studies of Manson<sup>22</sup> on tropical sprue. Later Goldberger<sup>13</sup> proved that in both man and animals the oral lesions of pellagra could be caused by a lack of some heat stable constituent of yeast and could be cured by supplementing the deficient diet with the missing factor. In a study of chronic canine black tongue, a deficiency disease of dogs, etiologically and symptomatically like pellagra in man, Rhoads and Miller<sup>32</sup> produced marked atrophic and inflammatory glossitis. The lesions disappeared promptly after a good source of vitamin B (yeast, or liver extract) was added to the deficient diet.

In 1932, Castle and Rhoads<sup>6</sup> published a preliminary report of an extensive study of tropical sprue in which the changes of the oral mucous membranes were used as an index of effective treatment. Later these same authors in a complete report presented evidence that the stomatitis of sprue, pellagra, and pernicious anemia are manifestations of a dietary deficiency of some constituent, similar in distribution to the heat stable vitamin B complex.

This thesis was supported by the work of Oatway and Middleton<sup>30</sup> and of Hutter, Middleton and Steenbock,<sup>15</sup> in which further experimental and clinical evidence was advanced to substantiate the view that one group at least, of inflammatory and atrophic lesions of the mouth were caused by a vitamin B deficiency and were curable by foodstuffs rich in that complex. The lingual manifestations of nutritional deficiency are illustrated in a publication by Minot and Castle.<sup>25</sup>

† We have employed for this purpose, Fleischmann's Dried Granular Brewer's Yeast, No. 2040.

undoubtedly more prevalent and of more importance in the etiology of mouth cancer than any other single form of chronic irritation and possibly of greater significance than the sum total of all other etiological factors.

We believed, therefore, that a survey of the dietary habits of patients with precancerous changes in the mouth, and also of those with intra-oral cancer, might reveal a high percentage of diets which were inadequate in vitamin B. We consequently undertook a systematic investigation of the diets of three parallel series from our clinic: Series I: 100 patients with precancerous stomatitis; Series II: 100 patients with fully developed mouth cancer; Series III: 100 normal controls (patients or their relatives) without any demonstrable complaint or lesion in the oral cavity.

An analysis of the dietary histories in these groups supported our theories in fact although not to the degree which we had expected. Nevertheless, the beneficial effects of vitamin therapy are incontestable in a large percentage of patients with intra-oral cancer or precancer, even though in some of them no deficiency can be demonstrated by the dietary histories or by any laboratory test thus far devised.

#### NATURE OF THE VITAMIN B COMPLEX

In the early days of vitamin research, vitamin B was thought to be a single substance, but later investigation has revealed that the B complex consists of from seven to twelve separate fractions which occur in association in foods in the natural state. The best known vitamin B fractions are B<sub>1</sub> (thiamin), B<sub>2</sub> (riboflavin), P-P (nicotinic acid), B<sub>6</sub> (pyridoxin), and pantothenic acid. Other components thought to be a part of the B complex are B<sub>3</sub>, B<sub>4</sub>, B<sub>5</sub>, factors L<sub>1</sub>, L<sub>2</sub>, U, vitamin M, para-aminobenzoic acid, the antigray hair factor and choline. The respective rôles of all of these substances in the maintenance of health in human beings have not been determined as yet; investigations on the more recently discovered fractions have been confined largely to animal

experiments. In Table 1 are listed the known functions of the B components, the symptoms of their deficiencies, and the average minimum daily requirement in healthy adults. It should be noted that these minimal amounts for normal persons are far below the therapeutic dosage necessary in well established cases of vitamin deficiencies. The reasons for this apparent discrepancy will be discussed later.

riboflavin are leafy green vegetables such as kale, spinach, turnip greens, carrot tops and beet tops, dried prunes, cheese and milk. Nicotinic acid is provided in lean meat and poultry, leafy green vegetables, milk, tomatoes and wheat germ. Pyridoxin is found in raw egg yolk, butter, nuts and cheese. The B complex does not occur in standard quantities in natural foods. Two different crops of the same vegetable may

TABLE I  
THE VITAMIN B COMPLEX

Factor	Function	Symptoms of Deficiency in Man	Average Minimum Daily Requirement for Adult
B <sub>1</sub> (thiamin)	Concerned with carbohydrate metabolism	Polyneuritis	1 mg. (300 I.U.)
B <sub>2</sub> (riboflavin)	Maintains integrity of the oral mucous membranes	Cheilosis, perleche, lesions at corners of mouth, eyes, and nose	2 mg.
B <sub>3</sub> (nicotinic acid)	Maintains integrity of nerve function, concerned in skin and oral mucous membrane nutrition	Pellagra—dermatitis, stomatitis, gastrointestinal disturbance, dementia	10 to 20 mg.
B <sub>6</sub> (pyridoxin)	Fatty acid metabolism? Maintains integrity of myoneural junctures? Prevents aerodynia dermatitis in rats	Nervousness, insomnia, difficulty in walking, myotonia?	Not known
Pantothenic acid B <sub>7</sub> (Williams-Waterman factor)	Prevents dermatitis in chicks Concerned with bird weight maintenance	Not known Not known	Not known Not known
B <sub>8</sub> (Reader factor) B <sub>9</sub> (Peters factor)	Rat paralysis preventative Concerned with pigeon weight maintenance	Not known Not known	Not known Not known
Factors L <sub>1</sub> and L <sub>2</sub> Factor U	Laetation factors for rats Growth factor for chicks	Not known Not known	Not known Not known
Vitamin M	Prevents nutritional cytopenia in monkeys	Not known	Not known
Antigray hair factor Para-aminobenzoic acid	Prevents gray hair in rats Concerned with bacterial metabolism	Not known Not known	Not known Not known
Choline	Prevents fatty liver in rats and dogs, perosis in chicks, and focal hemorrhages in the kidney of rats	Not known	Not known

Although liver and yeast are the outstanding sources of the vitamin B complex as a whole, other foods contain varying amounts of the separate B fractions. For instance, good sources of thiamin other than yeast and liver are lean pork, soy, lima and kidney beans, nuts, whole grains and egg yolk, while the best sources of

contain varying amounts of thiamin, riboflavin, nicotinic acid, etc. In addition, methods of processing and of cooking affect the fractions in different ways.

The daily minimum requirement of each of the B components for individuals is dependent upon several factors. It is known that since thiamin is related to carbo-

hydrate metabolism, persons whose diets are composed largely of carbohydrates will require greater amounts of thiamin. The need for this fraction is also increased directly with body weight.

Since the several B fractions occur in such close association, a proved deficiency in one is strong presumptive evidence of a deficiency in all the others although the symptoms may differ in character and degree. Some investigators have found that in certain sections of the country, because of dietary habits or unavailability of certain foods, there is more evidence of a deficiency in one factor of the complex than in the others, and that the administration of a crystalline form of this one factor will give fairly successful therapeutic results. This is particularly true in the pellagra districts of the South where nicotinic acid has been found to relieve most of the neuropsychiatric and dermatologic symptoms of the disease. In the northeastern states, however, the symptoms and signs of a deficiency which in many respects resembles pellagra, have, in our experience, never been relieved by nicotinic acid alone. Satisfactory results among our patients have been obtained only by administering some crude preparation like brewer's yeast, which contains in its residue, after isolation of the known components, some unknown or not clearly identified factors which are apparently essential to good health.

#### SIGNS AND SYMPTOMS OF AVITAMINOSIS B

The abnormal changes which result from an inadequate intake of the vitamin B complex are both objective and subjective. The sites and characteristics of the local signs and general symptoms may vary widely. Such variations could be due to differences in the individual's reaction to deficiencies of a given B fraction, or to differences in an individual's requirement of a given fraction, or to differences in the make-up of deficient diets. The variation in symptoms could also be explained, at least in part, by a synergistic action of the

B components, assuming that an absence of one interferes with the effect of the others. It is plain that the mental depression of a thiamin deficiency would naturally be accompanied by a loss of appetite and a lowered general state of health, which in turn would interfere with the absorption and metabolism of all ingested vitamins. Similarly, an inadequate intake of riboflavin with the characteristic mucous membrane lesions would result in a loss of appetite and, therefore, a diminished diet and vitamin intake.

Characteristic symptoms of an insufficiency in a single fraction can be produced with fair regularity in human beings, but such specific deficiencies can never occur spontaneously, since the several factors of the B complex are always associated in foods in the natural state. Because of such overlapping of the various causes and effects, no particular attempt will be made in the following discussion to identify the specific component of the B complex directly responsible for each symptom. The symptomatology in general will be considered as it applies to the problem of intra-oral cancer.

*General Symptoms.* In the taking of histories, it is often difficult to elicit from the patient such symptoms as constipation, anorexia, asthenia, dermatoses, onychodystrophy, mucous membrane changes and psychoneuroses, when present in mild degree, since he often does not recognize their existence until they have been relieved under treatment. In many published reports there has been a tendency to overlook the causal relationship and the full significance of such apparently unrelated symptoms as insomnia, malnutrition, stomatitis, etc. When considered from the standpoint of the specialist (dermatologist, psychiatrist, nutrition expert, cancer surgeon, etc.) the importance of a certain group of symptoms may be properly emphasized to the partial exclusion of the others. In this connection, we acknowledge that in the present report we are concerned mainly with the lesions in the oral mucous

membranes and their relation to precancer and cancer.

**Malnutrition.** One of the most common but by no means constant objective symptoms of vitamin B deficiency is malnutrition. This disorder is probably due to a combination of causes, anorexia and a lessened food intake with a decreased metabolism of carbohydrates as well as a general lowering of the state of health. Some patients may exhibit practically all of the symptoms of avitaminosis B (mental depression, stomatitis, dermatoses, etc.) associated with moderate or slight overweight. On the other hand, one of the most striking responses to vitamin B therapy is weight gain. (In Series I, or the stomatitis group, referred to in this report, there was some weight gain in forty-nine patients—51 per cent—the average gain was twenty-five pounds, the greatest gain in any individual being thirty-nine pounds.) When malnutrition is present in avitaminosis B, it tends to be marked and progressive.

It is erroneous to assume that malnutrition in patients with mouth cancer is due only to the difficulty and discomfort in taking food. While these obstacles play a prominent rôle, nevertheless, forced feeding to the point of tolerance, by mouth or by nasal tube, of from 3,500 to 4,000 balanced calories a day will often have little effect on a patient's weight unless provision is made for an adequate vitamin intake. For this reason, such diets should contain generous amounts of purees of green vegetables, supplemented by either natural vitamin B concentrates such as yeast or liver or synthetic preparations.

It is doubtful whether any exact standards can be set up for correlating the proper body weight with any combination of height, age and sex, although tables of such averages have been approximated which are useful in physical education. It is common observation, however, that marked variations from the average state of nutrition are compatible with good health and that such departures from the norm are often found in persons who possess to an

unusual degree, such qualities as physical and mental vigor and longevity. While leanness often seems to favor a long life, nevertheless, malnutrition constitutes a definite hazard when associated with a long and debilitating illness such as cancer.

**Neuropsychiatric Symptoms.** All investigators have noted the frequency of nervous and mental disorders as a part of the symptom complex in avitaminosis B. Jollisse<sup>17</sup> has recently discussed this subject in considerable detail. In this connection it is of interest to mention the experiment of Williams and Mason.<sup>18</sup> They obtained eleven female volunteers, who agreed to live in the hospital on an accurately measured and controlled diet, which was normal in all respects except that it was inadequate in thiamin. The subjects for this experiment were selected because of their willingness to co-operate, their previous satisfactory diets and the absence of any marked physical or emotional abnormalities. After a few weeks on this inadequate diet, all the previously normal volunteers became depressed, irritable, quarrelsome, and unco-operative, and developed other personality changes. These neuropsychiatric symptoms progressed to such a degree that finally open rebellion against the routine was threatened. The disturbance was immediately relieved and the subjects returned to normal when adequate thiamin was added to the diets.

The practical analogy between this experiment and the management of an apprehensive and nonco-operative cancer patient should be obvious. To the less intelligent person, a diagnosis of cancer is often equivalent to a death sentence, and even the best informed knows that with the exception of superficial cancer (such as cancer of the skin and lip), the over-all cure rate is not as high as 50 per cent, in other words, there is not an even chance for survival. Such melanoholic speculations in themselves naturally tend to produce mental depression, but the despondent mental state in patients with mouth cancer is not necessarily due solely to such morbid

reflections. If avitaminosis B is present in most cases as a precancerous condition, then the worry and apprehension accom-

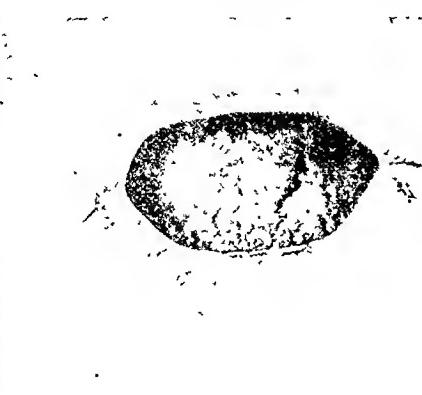


FIG. 1. *Perleche* in a female, aged sixty-two, who had complained of crusting and fissuring at the labial commissures for a period of one month. There was also a marked degree of hypertrophy and agglutination of the papillae, and fissure folding of the mucosa of the tongue (scrotal tongue).

panying the knowledge, or the suspicion of cancer, would be superimposed upon a pre-existing mental depression caused by a long-standing vitamin B deficiency.

One of the common accompaniments of mental depression is cancerphobia, which causes great distress to those so afflicted. The tendency of such harassed individuals to seek medical advice for such lesions as are definitely precancerous is obviously salutary. On the other hand, many neurotic patients complain bitterly of painful or burning sensations in the tongue but show no objective signs of abnormality. Although most of these probably suffer from avitaminosis B, the underlying nature of the disorder is not often recognized; and because of their repeated complaints, they constitute minor nuisances to their families and associates. A typical example of such a symptom complex is the following case report:

CASE I. M. J., a male dentist, aged thirty-seven, applied in March, 1940, for advice concerning a "sore" tongue of several months'

duration, which he feared to be cancerous. He slept poorly and worried a great deal, and he ascribed these nervous symptoms to marital discord which had progressed to the point where he considered a divorce the only solution. Objectively, there were only moderate changes in the tongue. The papillae were slightly hypertrophied and there was some lessening of the normal furring at the borders of the tongue. In a casual examination, with no complaint on the part of the patient, such a tongue would probably have been passed as normal.

The patient was assured that he had no sign of cancer, the probable nature of his disorder was explained, and he was advised to take large quantities of green vegetables and three tablespoonfuls of dried granular yeast daily. Two weeks later he returned for re-examination in a much more cheerful frame of mind. There was moderate improvement in the appearance of his tongue. He had gained five pounds, his bowels moved twice a day, and he had come to realize that previously he had been constipated. Guarded inquiries regarding his marital difficulties brought forth the rather embarrassed statement that since the improvement in his "disposition," these troubles had completely disappeared. He was advised to continue the vitamin therapy and corrected diet. When seen again after a few months, there had been no recurrence of the mental or oral symptoms.

*Perleche, Cheilosis and Generalized Dermatosis.* As first described by Sebrell and Butler,<sup>34</sup> one of the objective symptoms of a deficiency of the vitamin B complex, is a scaly, crusted, fissured erythema at the labial commissures (Fig. 1), sometimes extending for a short distance onto the vermillion border of the lips (cheilosis). This symptom, as well as the attendant mucous membrane changes, is thought by some observers to be the result of a deficiency in riboflavin, although Goldberger,<sup>13</sup> Jolliffe,<sup>16</sup> Manson-Bahr,<sup>23</sup> Drazin,<sup>9</sup> and others, consider a lack of nicotinic acid to be the important factor. It seems doubtful to us that the explanation of this lesion is so simple, since in a few instances we have observed perleche to develop first and to persist in patients who were receiving

massive doses of riboflavin (20 mg. daily) as part of their treatment for deficiency stomatitis. Such observations suggest that caution is necessary in attributing any specific lesion or symptom to a deficiency in a single fraction of the vitamin B complex. In our experience, neither perleche nor any other single symptom has responded as well to the administration of a particular B factor, as to a combination of several components or to such natural concentrates as yeast or liver.

Cheilosis often appears to include a disorder of the mucous and minor salivary glands of the lip, characterized by a sticky viscous secretion which, when dried, forms a brownish line on the lips. In aggravated cases, the mucous membrane has a finely mottled appearance marking the duct openings of the inflamed glands. In our experience, neither perleche nor cheilosis are precancerous lesions in themselves, but they usually indicate the presence of other degenerative changes within the mouth on the tongue or cheeks, which at these sites are precancerous.

In some instances a dermatosis of the same origin is more widespread, affecting the skin about the alae of the nose, the ears, the cheeks, the dorsum of the hands and fingers, or even the entire body. In pellagra, dermatoses are a characteristic symptom, beginning first, according to Spies, Hightower and Hubbard<sup>35</sup> as an erythematous area somewhat resembling sunburn which later changes to reddish brown. After desquamation, the skin seems to be abnormally red and thickened and permanent pigmentation may develop following frequent recurrences of the dermatitis.

*Onychoclasia, Fragilitas Unguium and Onychodystrophy.* Fragility and dystrophy of the fingernails are among the earliest and most common dermatologic manifestations of a vitamin B deficiency. The patient is sometimes unaware of these disorders until they begin to improve under specific therapy, as is also the case in the subclinical symptoms of constipation, anorexia and asthenia of deficiency disease. It is signifi-

cant that in a large percentage of patients with obvious mouth lesions of avitaminosis, guarded inquiries concerning the condition of the fingernails will elicit an admission that the nails tend to break easily (onychoclasia, fragilitas unguium). Other patients will insist that the nails and hair grow faster after vitamin B therapy.

Objectively, in cases of mild vitamin B deficiency, the nails may present longitudinal reeding, while in marked avitaminosis, onychodystrophy may appear in the form of transverse corrugations indicating variations in the rate of nail growth. From the practical standpoint, when there is some question as to the origin of mild disorders of the mucous membranes and/or malnutrition and asthenia, these abnormalities of the fingernails are of value as corroborative signs in the differential diagnosis of avitaminosis.

*Oral and Pharyngeal Symptoms.* In addition to the general and systemic symptoms already mentioned, there are inflammatory and degenerative changes of the oral and pharyngeal mucous membranes which are among the most common and most important manifestations of avitaminosis B. These degenerative changes are the result of subacute and chronic inflammation. There are several forms and combinations of these mucous membrane lesions, the particular variations probably depending upon the time intensity ratio, that is, slight deficiencies existing over a long period of time would undoubtedly produce different types of lesions (atrophy, leukoplakia, etc.) from severe acute deficiencies existing over shorter periods (acute inflammation, ulceration). In a few cases, we have been able to observe the progressive development of such degenerative changes in previously normal oral mucous membranes. (Fig. 2.)

Prior to the more recent discoveries in deficiency diseases, Oatway and Middleton<sup>30</sup> reported the occurrence of abnormalities of the tongue and mouth, in a variety of disorders including hypo- and hyperchlorhydria, gastric ulcer and cancer. Most of the mouth lesions which they describe

can be explained on the basis of an underlying or associated avitaminosis B. Spies, Hightower and Hubbard<sup>35</sup> and Rhoads and

inflammation or of the ulceration which is sometimes found in acute vitamin B deficiencies.



FIG. 2. The progressive development of degenerative changes of avitaminosis B resulting finally in scrotal tongue. S. G., male, aged thirty-two, was first seen in November, 1933, complaining of mild burning sensations in the tongue. The nature of the disorder was not recognized and there were no definite lesions observed in the tongue. The symptoms continued and a few months later mild inflammation and hypertrophy of the papillae were noted. *a*, The condition was then recognized as probably being due to a dietary deficiency and he was placed on vitamin therapy.

The patient was then lost to observation for a period of eight years after which he returned with aggravated symptoms (sore tongue, loss of weight, asthenia, mental depression). Neuro-psychiatric symptoms were such that he had become emotionally unstable and burst into tears during the interview. Marked progressive changes had occurred (scrotal tongue). *b*, He was directed to take 45 Gm. of granular yeast daily, and within a month he had gained about ten pounds in weight. The asthenia, mental depression and subjective symptoms in the tongue had completely disappeared.

Miller<sup>32</sup> have described in considerable detail the oral mucous membrane changes which accompany this form of deficiency disease.

**Glossodynias.** The chief subjective symptom in the mouth in avitaminosis B is pain, a burning sensation, or soreness of the tongue and sometimes of the cheeks or gums. Some patients complain of a constant dull pain chiefly in the tongue while the organ is at rest. Others find that hot or acid foods cause local discomfort. This hyperesthesia is a natural consequence of

In milder chronic avitaminosis B, pain or burning of the tongue may be a prominent symptom with little or no evidence of any mucosal abnormality. For this complaint the term *glossodynias* has long been used. Although it has been suspected that the condition was due to more than one cause, it has remained one of the minor unsolved medical problems. Some investigators have doubted that *glossodynias* represents a disease *sui generis*, and as Fox<sup>12</sup> found in his series, most of the patients are "chronic worriers." It is now obvious that most of

these cases are due to avitaminosis and that the symptoms can be completely relieved by vitamin therapy. From the point of view of cancer diagnosis, it is significant that one of the aggravating factors in almost all cases of glossodynbia is an associated cancerphobia.

*Inflammatory Hyperemia of the Mucous Membranes.* The basic response of the oral mucosa to a vitamin deficiency is chronic inflammation which closely resembles in appearance that produced by toxic, chemical, bacterial, traumatic or thermal agents. Although in a vitamin deficiency, there is no sound theoretical basis for assuming the existence of an irritant, we shall nevertheless use the terms *irritant, irritation and inflammation* in discussing mucous membrane lesions of avitaminosis, since we know of no better term to describe this disorder.

In severe and protracted vitamin B deficiencies, the affected membranes—most often of the tongue, and sometimes of the cheeks, gums, and palate—are deeply injected and inflamed, and often tender or even painful. This lesion may be asymmetrical or almost unilateral in the cheek and palate. In acute cases the appearance of this inflammation in the tongue may be obscured by furring. In severe and prolonged cases there is usually a disappearance of the normal coating or furring with some degree of papillary atrophy, and the mucosa of the tongue may have a diffuse reddish tint as if stained by a dye. In moderate degrees of deficiency, the inflammation and/or the disappearance of furring may occur only at the borders and on the tip of the tongue.

Inflammatory hyperemia of the tongue, cheeks or gums in avitaminosis B is one of the most significant precancerous lesions because it indicates the presence of a marked degree of chronic inflammation. It is found in association with atrophy of the papillae and cancer more often than any other degenerative change.

*Ulceration.* This symptom usually occurs only in the acute or exacerbated

stages of the aforementioned inflammatory lesions. The ulcers may be either single or multiple, they lack specific features and are commonly situated on the edges of the tongue, less often on the cheeks and gums, and have a yellowish irregular base with only slight erosion. Their specific nature is proved by their prompt healing and the disappearance of all attendant systemic and nervous symptoms under vitamin B therapy. Acute ulceration of the tongue in deficiency disease is not often of great precancerous significance because its clinical course is seldom of long duration.

The following case report illustrates this syndrome and its response to treatment:

CASE II. A. H., a traveling salesman, aged fifty-one, was first seen in April, 1940. He had noted a painful swelling of his tongue six months previous. His physician had diagnosed the lesion as Vincent's ulcer and had treated him by several intravenous injections of neoarsphenamine. This therapy at first produced improvement in the local symptoms but several subsequent attempts were not so successful and relapses and exacerbations occurred. The Wasserman blood tests were negative. About two weeks before admission the tongue became acutely sore with the appearance of several ulcers on the borders. At about the same time the patient developed acute insomnia, nervousness and mental depression. Arsphenamine therapy produced no improvement. Another physician had been called into consultation and the possibility of cancer discussed with the patient and his family.

At the time of the first interview the patient was in a highly emotional and apprehensive state, ostensibly because of the fear of cancer, and he obviously was having difficulty in restraining himself from weeping. He stated that his best weight was 156 pounds; his weight on admission was 148 pounds. This loss he ascribed to the recent increased soreness of his tongue and the consequent difficulty in eating. He admitted that due to the nature of his business as a traveling salesman, his dietary habits had been irregular. He was a moderate user of alcohol and had himself noted that the severity of his symptoms varied directly with the amount of alcohol consumed.

Local examination revealed the tongue to be slightly swollen with a moderate inflammation of the mucosa of the edges of the anterior half.

pernicious anemia, the significance of this symptom has been emphasized. In recent years, the discoveries of the nature and



FIG. 3. Ulceration of the tongue in avitaminosis B. (Case II).

Mainly on the right, but also on the left, there were several localized, superficial, yellowish ulcers surrounded by local swelling. (Fig. 3.) These lesions resembled herpes and varied from 3 to 5 mm. in diameter.

The patient was directed to take one teaspoonful of liver extract powder and one tablespoonful of dried granular yeast three times a day. Within one week, there was complete healing of the ulcers of the tongue and disappearance of subjective symptoms. Two weeks from the beginning of treatment he stated that his general health was much better, that he slept well and was more active in his business than formerly. At this time he weighed 163 pounds (a gain of fifteen pounds) and his appetite had improved to the point where he feared that he ate too much. One year after admission he was still taking three tablespoonsfuls of granular yeast a day. He had experienced no return of local or general symptoms and weighed 166 pounds, the total weight gain being eighteen pounds.

Superficial chronic ulceration and erosion of the mucous membrane is often found in association with "bald" tongue, or complete papillary atrophy, and with leukoplakia, as described in the succeeding paragraphs.

*Atrophy and Hypertrophy of the Papillae of the Tongue.* The frequent association of bald tongue with severe chronic anemia has been noted for at least a century, and in all of the earlier investigations on

effects of vitamin B deficiency have indicated that so-called pernicious anemia is also a deficiency disease, probably of the B complex, and that the glossitis and papillary atrophy of pernicious anemia is identical in origin with that found in sprue, pellagra and the common forms of precancerous changes in the mouth.

The velvety furred appearance of the normal tongue is due principally to the finer or filiform papillae and, as Middleton<sup>24</sup> and others have pointed out, in cases of atrophy, these filiform papillae are the first to disappear; the most obvious effect being a decrease in the furring and an increase in the solid pink color of the tongue. As these filiform papillae disappear and the inflammation continues, the larger fungiform papillae, fewer in number, become more evident. Gradually they become shorter, and the surface of the mucous membrane is at first finely pebbled, then becomes progressively smoother and finally bald. (Fig. 4.) An almost identical picture of atrophy occurs in chronic syphilitic glossitis. Bald tongue, when found in association with acute inflammatory hyperemia, is one of the most serious precancerous lesions in the mouth.

In some cases, especially in the milder forms of chronic inflammation (associated with avitaminosis, syphilis and particularly tobacco) there is a combination of atrophy

and hypertrophy so that while the papillae are obviously fewer in number, those which remain are increased in length and thickness. This condition produces a decrease in the furring of the tongue and results in a coarser or less velvety surface. In some instances, the hypertrophy is so marked that when the papillae are separated at any point, an apparent fissure 3 to 5 mm. deep runs down to their bases. These greatly hypertrophied papillae may later become agglutinated over irregular patches and the surface of the tongue coarsely pebbled. In such hypertrophic glossitis, the furring may be brownish in color. (Fig. 5.) Hypertrophy of the papillae is less often found in association with cancer than is atrophy.

Many authors speak of a re-growth of the papillae under specific therapy. In our experience, such regeneration takes place only in the early stages when the atrophy is slight or partial. The lesion of advanced or complete atrophy of the papillae is not reversible and although all acute and subacute inflammation may disappear, the tongue remains bald.

*Fissure Folding.* This lesion which has sometimes been called "scrotal tongue" is the result of swelling of the mucosa and submucosa, and possibly also of the musculature (interstitial glossitis) so that the tongue becomes too large for the closed oral cavity. Consequently, the organ is compressed and the hypertrophied mucosa and submucosa are forced into folds which become evident as deep, nonulcerated fissures when the mouth is opened and the pressure released. The surface of the tongue then presents an irregular striated appearance. (Fig. 5.)

*Leukoplakia.* The most common oral lesion resulting from one or more forms of mild, long-standing, chronic irritation is leukoplakia. On close examination, some leukoplakia can be demonstrated in about 50 per cent of all males and in about 10 per cent of all females over forty-five years of age. In clear cases of avitaminosis it is usually impossible to state with assurance that an associated leukoplakia has been

caused by the deficiency alone, or by a combination of other factors such as smoking, syphilis, etc. The leukoplakic patches may



FIG. 4. Complete papillary atrophy or bald tongue. B. C., female, aged seventy-nine, with a history of sore tongue of five years' duration. The projection to the left of the midline on the dorsum was removed for histological examination and proved to be benign papilloma.

be small, superficial and present only on the mucosa of the cheeks just back of the labial commissures, or they may be widespread over the mucous membranes of the oral cavity (cheeks, tongue, palate, etc.). When the dorsum of the tongue is affected, there are often irregular thickened patches dispersed on a bald surface. (Fig. 6.) It is this clinical picture to which the term "lingua geographica" is usually applied.

The milder degrees of leukoplakia are of significance from the standpoint of pre-cancer only in that they indicate the existence of chronic irritation. The thickened, fissured, or ulcerated patches of leukoplakia are of more immediate significance in that they may actually be undergoing malignant degeneration. Leukoplakia is not often found in association with the acutely inflamed bald tongue. We have observed cases of patchy striated leukoplakia of the oral mucous membrane associated with dermatoses and previously diagnosed by a dermatologist as lichen planus, which responded to vitamin B therapy.

*Gingivitis.* The most frequent symptom of a mild gingivitis is bleeding from the gums on brushing the teeth, which of

deficiency stomatitis. In some aggravated cases the gums are swollen, deeply injected, and tender or painful on mastication. Al-



FIG. 5. The clinical picture of *scrotal tongue*, illustrated by Figures 5a and b, is produced by a combination of hypertrophy, agglutination of the papillae and fissure folding



FIG. 6 *Leukoplakia*. A mild, long-standing glossitis of avitaminosis, or any other form of irritation, is likely to produce leukoplakia in association with other degenerative changes in the tongue. In this case the patient was a male, aged seventy-two, who had noted white patches on the tongue for a period of fifteen years. a, His diet was inadequate and he complained of chronic constipation. He was a heavy smoker, but the Wassermann test was negative. b, There was marked improvement under vitamin therapy.

course can occur in any form of gingivitis. Some degree of gingivitis is almost always found in even the mild stages of vitamin

though the lesion is supposedly more characteristic of avitaminosis c (scurvy), it is probable that the most common cause of

gingivitis, as proved by specific therapy, is a vitamin B deficiency. This lesion is undoubtedly of precancerous significance in gum cancer.

It seems to us that most of the inflammatory lesions grouped under the vaguely defined terms of "trench mouth" and "Vincent's infection" are not primarily bacterial diseases but rather the inflammatory lesions of avitaminosis in which the Vincent's organisms, present in most mouths, are secondary invaders. King<sup>18</sup> has reported the successful treatment of Vincent's infection with nicotinic acid. Williams,<sup>39</sup> in discussing the prevalence of Vincent's angina among Mexican patients, calls attention to the fact that their diets were habitually inadequate in vegetables and fruit, and he believes that the deficiency was mainly one of vitamin C. Topping and Fraser<sup>37</sup> and Tomlinson<sup>36</sup> produced mouth lesions in monkeys varying from a mild gingivitis to complete gangrenous necrosis of the cheeks by feeding the animals diets lacking in the vitamin B complex.

In some cases gingivitis may be the preponderant symptom of avitaminosis B with relatively few or even no objective findings in the tongue or mucosa of the cheeks. In these instances the gingivitis may go on to the formation of bulky granulomas as in the following case report:

CASE III. H. C., schoolgirl, aged seventeen, was first seen in March, 1937, with a history of pain and swelling in the left upper gum, of seven month's duration. One month previous to the first interview, several teeth in the left upper jaw became loosened and her dentist discovered a granular tumor in this area. Examination revealed an edematous swelling of the left upper gum, 3 cm. in diameter, extending onto the hard palate. The mucous membrane in the affected region was deeply injected, but not tender, and the rest of the gums were fairly normal. A biopsy was reported as *plasma cell granuloma*. The other clinical and laboratory examinations, including roentograms, were negative.

Under a diagnosis of granulation tissue epulis, the teeth were extracted and the tumor removed locally with curettage and cauteriza-

tion of the base. Eight months following the operation, the patient reappeared with marked swelling in the subcutaneous tissue of the right cheek and of the right upper and lower gums. Local measures had failed to give relief.

At this time it was suspected that the disorder might be systemic rather than local and therefore she was given liver extract powder, two teaspoonsfuls three times a day. In two weeks the gums had practically healed and the swelling in the cheek had disappeared. The liver therapy was continued for several weeks, and then as an experiment, it was stopped and the patient was given nicotinic acid (50 mg. daily). After a few weeks on the latter form of therapy, her gums had again become sore, she had lost fifteen pounds, and her menstrual cycle had become irregular.

She was then placed on vitamin B therapy (Vegex) and within a few days the soreness of the gums had subsided. She soon regained her lost weight and the menses returned to normal. Since that time she has experimented with several forms of vitamin B therapy, under our direction, but she reacts best to liver extract powder. If she stops taking the liver, she immediately begins to lose weight and the gums become sore. It is noteworthy that in this case relief can be obtained only by the use of crude concentrates and not by a single fraction of the B complex such as nicotinic acid.

*Salivary Changes.* In severe prolonged deficiencies of the B complex, the mucous membranes of the mouth appear to be drier than normal with a loss of normal gloss and with a brownish tint in the furring of the dorsum of the tongue. The saliva is lessened in quantity and increased in viscosity. The cause of this abnormality may be, in part, a decrease in the volume of saliva secreted by the parotid and submaxillary salivary glands as the result of malnutrition, lack of appetite and decreased fluid intake. It is probable, however, that this symptom is due also to a disorder of the minor salivary and mucous glands, which are numerous in all of the oral mucous membranes and whose secretions lubricate and moisten the mucosa. One of the most characteristic responses to vitamin B therapy is the disappearance of the brownish color in the mucous membranes and the resumption of

their usual pale, pink, glistening character when the salivary secretions return to normal.

*Plummer-Vinson Disease.* The lesions of this syndrome (esophagitis, dysphagia, spasm of the pharyngo-esophageal sphincter, anemia, glossitis) were originally believed to be present only in the esophagus, but more recent investigation has revealed that they usually effect the mouth and pharynx as well. It is found more often in women than in men, and especially in Sweden where Ahlbohm<sup>1</sup> has established the fact that it is definitely a precancerous lesion. Hypoproteinemia and avitaminosis B are associated as the main etiologic factors. Since the lesions almost always improve or disappear following the administration of a high protein diet supplemented by vitamin B, the disorder is undoubtedly a deficiency disease.

A typical example of this syndrome came under our observation several years ago in a woman of sixty years, with advanced esophagitis, sore mouth, malnutrition and neuropsychiatric disturbances. She habitually consumed between one and two quarts of gin daily and often went for periods of several days without taking any food whatever. At that time we did not suspect the deficiency nature of the disease and therefore she did not receive vitamin therapy. While in the hospital under observation for the cause of her esophagitis she improved markedly on the regular hospital diet with a reduction of the alcohol consumption. After leaving the hospital she resumed her former habits and died within a few months, ostensibly of chronic alcoholism. It is now plain to us that the basic cause of death in this case was complications of a severe vitamin deficiency.

*Lesions of the Mucosa of the General Gastrointestinal Tract.* While the most pronounced local subjective and objective mucous membrane symptoms occur in the mouth, these abnormal changes undoubtedly involve other portions of the gastrointestinal tract. The abundant sensory nerves of the oral cavity and the ease with

which the mouth can be examined probably give an exaggerated picture of localization of these lesions in this area. Nevertheless, the appearance of the tongue has long been considered an index to the health of the rest of the alimentary canal. As Lewis<sup>19</sup> has remarked, "Raw red tongue, raw red gut."

In cases of stomatitis of avitaminosis B, such symptoms as anorexia, indigestion, malnutrition, and constipation, suggest the presence of mucous membrane abnormalities in the stomach and intestines. Mackie, Miller and Rhoads<sup>21</sup> and Plummer<sup>31</sup> have demonstrated roentgenographically altered motor activity in the small intestines as a result of a vitamin B deficiency and they have shown that these abnormalities improve after specific therapy. Mackie<sup>20</sup> notes that the changes which occur in the small intestine in deficiency states are similar to the conditions present in the intestine of the very young baby whose nervous system is immature. He believes that these deficiency patterns are caused by some impairment of the functioning of the nervous system of the small intestine, caused by avitaminosis. Golden<sup>14</sup> also attributes the intestinal dysfunction to damage to the intramural nervous system.

The evidence is plain for at least a tentative diagnosis of avitaminosis B when an inflammatory oral mucosal lesion is associated with one or more of the following symptoms: malnutrition, mental depression, nervousness, insomnia, constipation, dermatoses and onychodystrophy. It is an interesting field for speculation and further investigation as to whether the incidence of an associated stomatitis (indicative of a B deficiency) is not more frequent in persons suffering from esophageal, gastric and rectal cancer than in those not so afflicted. Such investigations are now in progress at Memorial Hospital.

#### DIFFERENTIAL DIAGNOSIS OF THE INTRA-ORAL LESIONS OF AVITAMINOSIS B

As we have previously mentioned, the various forms of acute and chronic degener-

ative changes in the oral mucous membranes produced by a deficiency in the vitamin B complex, are not peculiar to this

normal furring of the tongue is absent. The furred border of the lesion progresses outward at the rate of several millimeters a



FIG. 7. *Glossitis migrans*. Photographs a, b and c were taken at intervals of two to four weeks and illustrate the changing character of the lesion. Vitamin therapy gave little benefit.

condition alone, but in many respects are identical in appearance with those produced by other forms of chronic irritation. When a composite clinical picture has been produced by several forms of chronic irritation, the clinical history and laboratory tests (Wassermann, liver function, etc.) may be of assistance in determining the responsible agents, but the differential diagnosis must be based mainly upon the response to therapy (dietary, antileptic, etc.) or the effect of the elimination of the various suspected offenders (smoking, dental trauma, etc.).

There are certain clinical syndromes which should lead the observer to suspect a dietary deficiency and which should suggest a therapeutic vitamin test, for example, the atrophic tongue with injection of the mucosa and scanty, sticky saliva.

*Glossitis Migrans.* Although similar in some respects to the lesions produced by avitaminosis B, glossitis migrans is a disorder of the tongue of unknown origin which is seldom improved by vitamin B therapy. It consists of a sharply demarcated, heavily furred curved border of varying length, and about 3 to 5 cm. in width. Within the curve of this border the

day, parts of it tending to fade out at the edges. Other second or third linear lesions may arise and progress outward from the point of origin, so that sometimes there are as many as three visible arcs. In rare instances the curved linear border consists of intense inflammation with a fibrinous exudate rather than an increase in furring. If observed at intervals of two or three days, the appearance is never the same. (Fig. 7.) Some patients with this lesion feel better systemically under vitamin B therapy, but in our experience, this seldom has any effect on the local lesion.

#### FREQUENCY OF VITAMIN B DEFICIENCY IN PATIENTS WITH MOUTH CANCER

From the foregoing descriptions of symptoms and signs of avitaminosis B, it will be apparent that the clinical picture is not clear cut, and that it would be impossible to separate a group of individuals into two definite classes, one with conclusive evidences of vitamin B deficiency and the other with no evidence whatever. No laboratory test has been devised which furnishes an accurate basis for this determination. For this reason, there is as yet no method of determining the absolute inci-

dence of avitaminosis B in mouth cancer or precancer. The proof of such dietary inadequacy is found in the fact that a large percentage of patients with mouth cancer do manifest one or more of the general and local abnormalities, and that these are almost always improved by administration of vitamin B. In brief, although no statistical proof can be presented, it is undoubtedly true that most patients with mouth cancer are suffering from an inadequate intake of the B complex to some degree at the time of admission. As proved by the therapeutic test, the same is true of most patients with precancerous mouth lesions, and it is therefore probable that the mucous membrane changes of avitaminosis B are more common and of more importance than those of all the other chronic irritants combined.

#### AVITAMINOSIS B AS A PROBLEM IN THE TREATMENT OF INTRA-ORAL CANCER

If one accepts the postulates already outlined, that a majority of patients with intra-oral cancer have avitaminosis B on admission—a condition which existed prior to and was at least partially responsible for the development of the cancer—the relief of this deficiency is an important part of the treatment of mouth cancer. When the intra-oral growth extends and becomes infected, or when aggressive treatment is instituted, either surgically or radiologically, mastication and swallowing become painful, and the sense of taste and the appetite are lost so that there is little inducement for the patient to eat properly. The acidity of fruit and vegetable juices (one of the normal sources of vitamins) is irritating to the inflamed mucosa. The necessarily soft or liquid diet in these cases tends to grow progressively restricted, and if not medically, will in most cases finally consist mainly of milk and raw eggs.

As a result, practically all patients with intra-oral cancer eventually develop an avitaminosis, whether or not it existed in the beginning. As the local symptoms increase in severity, mental depression and

nervousness are aggravated. The best proof of the underlying cause of this train of symptoms is the almost certain improvement if not complete relief which follows an adequate vitamin intake.

In the patient with cancer, the depressing psychological effects of the knowledge or suspicion that he has cancer, is often the cause of more suffering than any organic effect of the malignant tumor. It is in these situations that vitamin therapy makes one of its most valuable contributions. A great deal has been written about the psychic management of patients with cancer, especially as to whether they should be informed of the true nature of their disease. Whether the patient is told the truth or merely suspects it, he will nevertheless be better able to face his misfortune with fortitude if he is not handicapped by the pessimism and melancholia which accompany avitaminosis B. In any disease as wasting and depleting as mouth cancer, the maintenance of proper nutrition is essential to successful treatment of the favorable cases as well as in palliation of the incurable.

#### DIETARY CAUSES OF AVITAMINOSIS B, OF PRECANCEROUS ORAL LESIONS AND OF MOUTH CANCER

We have maintained that the intra-oral lesions of avitaminosis B were precancerous and that some degree of avitaminosis was present on admission or developed during the course of treatment in practically all cases of intra-oral cancer. While these theories seemed perfectly sound to us from the empiric standpoint, we considered it only proper to test their validity by an investigation of the dietary habits of patients with intra-oral cancer and of patients with precancerous lesions of the oral mucous membranes, using as controls healthy persons with no intra-oral complaint. It was assumed that such a study would reveal whether an insufficient intake of the vitamin B complex, as shown by the dietary habits, was mainly responsible for the vitamin deficiency or whether such a

deficiency was due to an abnormally high individual requirement. This survey occupied a period of several months during which one of us (C. E. K.) interviewed some hundreds of patients with regard to their dietary habits, making a careful record of the presence or absence of intra-oral abnormalities.

Three groups were studied, care being taken to assure uniformity with regard to the average age and sex distribution. Series I consisted of 100 patients from the clinic with definite precancerous oral lesions of the oral mucous membranes, all of whom presented one or more of the objective findings already outlined in a previous section of this report. Since leukoplakia alone is present in such a large percentage of the population, no patient was included in Series I who did not present some specific precancerous lesion other than leukoplakia.

Series II consisted of 100 patients with cancer of the mouth chosen at random from the Head and Neck Clinic at Memorial Hospital.

Series III (controls) consisted of 100 patients from the clinic (mainly those with facial skin cancer or relatives of patients) who appeared to be in excellent health and whose oral mucous membranes were essentially normal.

#### RESULTS OF INVESTIGATION OF DIETARY CAUSES OF AVITAMINOSIS B

*Method of Survey.* The estimation of the vitamin content of a diet from history alone is subject to considerable error since the calculation must be made on hearsay evidence alone. The following safeguards were used in the present investigation: (1) Unhurried interviews, avoiding leading questions; (2) the use of low minimum standards of vitamin requirements; (3) separation of those with adequate diets from those with inadequate diets by interposing a suboptimal group. The latter cases were considered indeterminate and were not included in the final calculations; (4) an allowance for loss of vitamins by cooking;

- (5) estimation of food juices consumed, and
- (6) calculation of diets on a weekly basis.

Various types of foods were classified loosely according to their vitamin B content, for example, leafy green vegetables, roots, legumes, fruits, seeds, cereals, meat and milk products, respectively. During the interview a typical week's menu was obtained from each patient, and each was then asked specific questions about the various food groups contained in his diet in order to have a double check on his dietary history. Peculiarities and fads of diet were recorded.

The daily intake of thiamin was used as an indication of the vitamin content of the diet. This fraction rather than any other was selected because of its widespread use as a survey factor and because its average daily requirement has been more definitely established than those of the other B components. Although a calculation of  $B_1$  in the diet is not a highly accurate measurement of the other B fractions present, nevertheless, for our purposes it is a valuable indication of the general content of the vitamin B complex, with the possible exception of nicotinic acid.

The thiamin content of the individual diets was calculated in International Units according to the food values of Bowes and Church,<sup>3</sup> and two final calculations were made: First, the averages of the B intake in each of the three series were compared. Secondly, the percentage of adequate and deficient diets in each of the three series was calculated. In the latter calculation, the suboptimal group was omitted since we believe that this group contains a large number of borderline cases which had best be considered indeterminate.

*Standards.* The standard vitamin requirements of Munsell<sup>28,29</sup> were used, because of their wide acceptance and the fact that she employs as low a minimum requirement as any in common use. This low minimum serves to insure that diets considered low in the present survey are actually below the normal. In this manner, 2,100 International Units of  $B_1$  per week

was considered adequate. Since any exact minimal figure must be considered arbitrary, a suboptimal group was included, made up of diets between 2,100 and 1,400 units per week. Diets containing less than 1,400 units per week were classed as deficient.

On a weekly basis, then, the figures are as follows:

Adequate . . . . .	2,100 or more International Units $B_1$ (7 mg.) . . . . .
Suboptimal . . . . .	1,400 to 2,100 International Units $B_1$ (4 to 7 mg.) . . . . .
Deficient . . . . .	Less than 1,400 International Units $B_1$ (Less than 4 mg.) . . . . .

*Results of Dietary Survey.* As might be expected, the calculations of the vitamin content of these diets reveals considerable irregularity. The significant trend is seen in the averages of the whole groups and (excluding the suboptimal cases) in the relative numbers of adequate and deficient diets in each of the series. These averages are given in Table II.

In evaluating the clinical significance of these figures we have applied the statistical method as outlined by Campbell<sup>4</sup> and

found our figures to be statistically reliable; that is, the differences between the sets of percentages compared may be considered due to factors other than chance. Any figures derived from the suboptimal group had best be considered inconclusive, since the classification of a given diet as suboptimal may depend upon errors in the interpretation of the dietary histories or upon moderate variations in the individual's vitamin requirement. That the economic status of the patient is of some importance from the standpoint of adequate diet, was shown by the fact that in the stomatitis group there was a higher percentage of deficient diets among clinic patients than among private patients.

The similarity of distribution of adequate, suboptimal and deficient diets in the stomatitis and mouth cancer series seems to us to be strong indication that they have the same dietary habits, and that individuals with deficient vitamin B diets have a greater tendency to develop intra-oral cancer than those on adequate diets.

In an investigation of this kind many paradoxical cases will be found, and it is

TABLE II  
DIETARY SURVEY IN INTRA-ORAL CANCER AND PRECANCER\*

Group	Weekly Average	B <sub>1</sub> Intake			
		Percentage of a Given Series			
		Adequate B <sub>1</sub> Per Cent	Inadequate B <sub>1</sub> Per Cent	Suboptimal B <sub>1</sub> Per Cent	Deficient B <sub>1</sub> Per Cent
Series I (100 cases) . . . . .	1,690 I.U. (5.6 mg.)	30	70	47	23
Stomatitis					
Series II (100 cases) . . . . .	1,865 I.U. (6.2 mg.)	34	66	47	19
Intra-oral cancer					
Series III (100 cases) . . . . .	2,215 I.U. (7.4 mg.)	49	51	46	5
Normal controls					

\* The average weekly intake of vitamin B<sub>1</sub> in the stomatitis series (1,690 I.U.) and in the mouth cancer series (1,865 I.U.) is about 25 per cent less than that in the normal controls (2,215 I.U.).

Although about half of the controls consumed inadequate diets, only 5 per cent were definitely deficient. In the stomatitis and mouth cancer series 70 per cent of the diets were inadequate with over 20 per cent definitely deficient. In brief, definitely deficient diets appear to be about four times as frequent in the mouth cancer and stomatitis groups as in the normal controls.

plain that the existence of an avitaminosis cannot always be demonstrated by a survey of the dietary histories alone. In our Series III (normal controls) there were a number whose diets were definitely deficient, that is, containing less than 1,400 International Units of B<sub>1</sub> per week. Furthermore, in Series I among those patients who had advanced lesions of stomatitis, there were some patients who according to their dietary histories, were taking adequate diets, that is, 2,100 International Units per week or more. The true nature of the stomatitis in the latter type of case was demonstrated by the improvement and even complete disappearance of the symptoms when the intake of B was raised to several times the normal requirement. Such an instance is illustrated in the following case report:

**CASE IV.** J. F., a male cook, aged sixty-three, was first seen in October, 1937, with squamous carcinoma of the tongue. The growth was treated by radiation, regressed promptly, and has not recurred. When first seen there was an associated bald, deeply injected tongue, and as a part of his general treatment he was placed on routine doses of vitamin concentrates in the form of liver and yeast. Within two months after the beginning of treatment, he had gained twenty-five pounds in weight. The tongue remained completely bald after the radiation reaction had subsided. (Fig. 8.) The degree of injection varied inversely with the regularity with which the patient followed directions as to vitamin therapy.

About a year and a half after admission, his health seemed to decline, even though he had been consuming about three tablespoonsfuls of yeast daily, together with large quantities of leafy green vegetables. From this point onward, his condition became worse and no form of vitamin B therapy seemed beneficial until he increased his intake of yeast to eight tablespoonsfuls daily, a dose which few patients can tolerate without marked nausea and diarrhea. There was a consequent immediate improvement in the state of his oral mucous membranes and general health. Since that time he has continued on that dosage and we have found that if he temporarily discontinues or reduces the

amount of yeast, his appetite becomes poor, he loses weight and the tongue symptoms are aggravated.



FIG. 8. Completely bald tongue in a patient (Case IV) who had squamous carcinoma of the tongue, and other degenerative changes in the oral mucous membranes when first seen in October, 1937. The growth regressed after radiation and has not recurred.

When first examined, he had acute symptoms of vitamin deficiency, that is, deep injection of the tongue and perleche. He gained twenty-five pounds while on vitamin therapy. His health began to decline during the past year and it was found that unless he takes eight tablespoonsfuls of yeast daily, the symptoms become markedly intensified. Despite these high doses, his tongue remains completely bald with deep fissures at the angles of the mouth (perleche).

These cases in which massive doses of vitamin B must be taken in order to maintain health can be explained on the basis of marked individual variations in ability either to absorb or utilize ingested vitamins. Among those patients in the stomatitis and mouth cancer series whose diets we calculated as suboptimal (though not definitely deficient) there was actually a considerable number who presented unmistakable signs of avitaminosis, the explanation being that although their intake was not far below normal, their requirements were inordinately high.

Some investigators have suggested that nonabsorption of vitamins from the gastrointestinal tract may be caused by such disorders as enteritis, colitis, diarrhea, etc. Once vitamins are absorbed, it is thought that they are changed in chemical composition and their end products finally utilized in the liver. Disorders in liver function would, therefore, prevent the normal metabolism of these substances. Cowgill,<sup>7</sup> Bridges<sup>8a</sup> and others believe that the vitamin B<sub>1</sub> requirement varies in the individual with the rate of caloric exchange and increases with the body weight in febrile conditions, in hyperthyroidism and in pregnancy. Not all of these theories have been clearly substantiated experimentally.

*Dietary Peculiarities.* A review of the histories of patients in the stomatitis series reveals a curious collection of dietary abnormalities from a wide variety of causes. In some cases avitaminosis was brought on by medically prescribed but unknowingly deficient diets for such diverse conditions as peptic ulcer, gallbladder disease, obesity, colitis, etc. Some of these patients, convinced that an improper diet was the original cause of some particular disorder, had blindly followed an even more incorrect and vitamin deficient diet for a period of years, bringing on symptoms far more serious than the original ailment. In some instances the responsible physician had dropped out of the case; in others, he had continued to care for the patient and was himself unaware of the harm his treatment was doing.

Fad diets were common even among well educated and intelligent patients seen in private practice. Some of the fadistic tendencies were based on ideas original with the patient, others had come from radio talks and health columns in newspapers and magazines. In many cases there was evidence of a vicious cycle; that is, a dietary deficiency brought on a loss of appetite and lack of interest in food so that the patient progressively restricted his diet to those substances most easily and cheaply obtained, mainly pure carbohydrates. In

Table III are listed some of the peculiar diets in this group. We might mention in this discussion that dietary whims do not always lead to deficiencies, since among the normal controls we encountered a number of fad diets which were obviously adequate in vitamins and which included such habits as drinking the water in which potatoes were cooked, using only whole wheat flour for baking purposes, etc.

TABLE III  
INSTANCES OF ABNORMAL DIETS IN CASES  
OF AVITAMINOSIS

1. A wealthy eccentric usually ate only breakfast, and after that beer and onions when he was hungry.
2. A woman voluntarily accompanied her husband on a diet for his peptic ulcer.
3. A woman prescribed for herself a diet for gallstones.
4. A woman restricted herself to a 1,000 calorie diet.
5. A mortician ate no vegetables and had a phobia for certain meats and fowl.
6. A traveling salesman ate a diet deficient in quantity and usually consisting only of sandwiches because he feared dirty food.
7. A woman ate no food juices, fruits, nor eggs and was on a liquid diet for three weeks prior to the onset of the stomatitis.
8. A dentist followed a combination of successively prescribed diets to the extent that he ate only lamb chops, soda crackers, applesauce, plain cake and cream.
9. A man ate neither meat nor vegetables.
10. A female peddler ate bread, butter, eggs and fruit exclusively.
11. A paretic beer salesman drank beer when hungry.
12. A woman avoided pork, fruit, eggs and milk because two members of her family were on diets eliminating these foods. In addition, she limited herself to 1,000 calories a day in order to reduce.
13. Two patients followed medically prescribed reducing diets.
14. A nurse followed a self-prescribed diet for gastritis and peptic ulcer, the latter of which she did not have.
15. Three patients were on grossly inadequate diets because of their financial status.

It is probable that the most frequent underlying cause of an inadequate vitamin intake lies in individual personality factors such as peculiar dietary prejudices formed in childhood and often based on racial, nationalistic or provincial family customs. Idiosyncrasies are commonly met with in temperamental, impressionistic individuals, some of whom refer to all vegetables as "rabbit food." Such temperamental whims may be either the cause or the result of a

vitamin deficiency. When they are both, a vicious cycle is set up. In women, deficient diets are often due to the fear of gaining weight. In most city dwellers there is the tendency to eat at "quick lunches" and drugstore counters, where green vegetables and fresh meats are replaced by carbohydrates in the form of sandwiches, ice cream, malted milk and pastry.

*Chronic Alcoholism.* Since alcohol can be oxidized in the body to produce energy, and thereby replace carbohydrates and to some extent, fats, chronic alcoholics can live for considerable periods provided that they ingest minimal quantities of proteins to replace protein and mineral waste. The degree of chronic alcoholism is variable, since some patients replace only a part of their diets with alcohol. In any case, the energy-producing alcohol is almost a pure chemical and contains neither vitamins, proteins nor minerals.

It has long been believed by those engaged in vitamin research that the neuritis, some of the psychoses and other general effects of chronic alcoholism were mainly due to a vitamin B deficiency. The validity of these theories had been supported by the work of Minot, Strauss and Cobb,<sup>27</sup> who found that the neuritic symptoms of alcoholism could often be relieved by the administration of the vitamin B complex without any decrease in the consumption of alcohol or other increase in the vitamin content of the diet.

It has been our observation that the deficiency symptoms in chronic alcoholism sometimes consist chiefly of malnutrition and degenerative precancerous changes in the oral mucous membranes. It is our opinion that the significance of alcohol in the etiology of mouth cancer lies in its capacity to produce the stomatitis of vitamin deficiency rather than to its local irritative effect on the oral mucosa. The following case report illustrates our view:

CASE V. P. P., a male, aged sixty, first came under our observation because of epidermoid carcinoma of the posterolateral border of the tongue. At the time of the first examina-

tion, it was noted that the mucosa of the entire tongue was deeply injected with partial atrophy of the papillae along the edges and hypertrophy over the dorsum. The growth was treated by radiation and completely regressed, the patient remaining free of cancer for about eighteen months. He then developed a second primary lesion in the anterior floor of the mouth. This second primary was also treated successfully by radiation. The patient then remained free of local cancer until the time of his death two years later from pulmonary metastases.

During the three-year period between the first development of his tongue cancer and his death, he was under close observation and it was noted that the acute or subacute glossitis never completely disappeared. The inflammatory symptoms improved whenever the patient could be persuaded to take a reasonably adequate diet, supplemented by vitamin concentrates, but the glossitis always immediately became aggravated when his dietary habits returned to their customary irregular character. At such times the tongue would become acutely inflamed and tender and the saliva scanty and sticky. These relapses were accompanied by an increase in his psychoneurotic symptoms and a marked loss of weight.

In his youth he had inherited a large fortune which insured him of an adequate income and left him free to indulge the whims and erratic tastes of a constitutionally unstable personality. He was temperamental, strongly opinionated and prejudiced in his dietary habits and had an intense dislike for certain foods, especially green vegetables and meat. He was convinced that the most wholesome and entirely satisfactory meal for him was a raw egg with a glass of sherry twice a day. He had formerly consumed moderate amounts of whiskey, which his family physician had finally induced him to give up; but he continued to take generous quantities of ale and champagne, which, despite medical advice, he firmly believed to contain only a small percentage of alcohol.

Although he was five feet, eight inches tall, he stated that he had never weighed more than 120 pounds. While under treatment for his tongue cancer his weight varied between a high of 130 pounds on a carefully regulated diet, and a low of 110 pounds when he resumed his usual dietary habits. During the last three

years of his life, despite persistent medical attempts to correct his diet and vitamin intake, he became progressively more difficult to control and often rebelled for periods of several weeks, during which times he subsisted on minimal quantities of milk, raw eggs with sherry, ale and champagne. The stomatitis persisted, always becoming more severe at the times of reduced vitamin intake. There were progressive degenerative changes in the oral mucous membranes and it is probable that had he survived he would have developed a third or even more primary cancers of the mouth.

The association of causes and effects in this case seems rather obvious to us, that is, the inherent personality weaknesses leading to an unhygienic mode of life, sufficient wealth to obviate the necessity for any discipline or restraint in indulging the various whims and irregular habits including chronic alcoholism, avitaminosis, pre-cancerous stomatitis and finally multiple mouth cancers.

#### TREATMENT OF AVITAMINOSIS B

There is apparently little storage of excess vitamin B in the body beyond the current need, and deficiency symptoms occur within a few days after withdrawal of the vitamin source. For this reason, any effective treatment must be made part of a frequently repeated and regular routine. Furthermore, the quantities of the various fractions of the B complex necessary to prevent deficiency symptoms are specific for each individual. When a marked avitaminosis has developed, a partial remedial dose will have little effect on the condition, and relief will not be obtained until the full necessary amount is administered.

As we have already mentioned, there is a wide variance between the minimum requirements in health (which have been established experimentally) and the therapeutic doses necessary to obtain the maximum benefit in cases of spontaneous vitamin deficiency. For example, although 1 mg. of thiamin and 2 mg. of riboflavin have been found to be required for the maintenance of health in the normal adult,

these quantities when administered to a person suffering from severe avitaminosis, will rarely produce the maximum beneficial effect, and in most cases will not cause any noticeable improvement.

We have found it advisable, when using natural concentrates such as yeast and liver, to provide from five to ten times the normal minimum requirement of thiamin and riboflavin, or 30 to 45 Gm. (2 to 3 tablespoonfuls) daily of granular yeast. In exceptional cases the maximum relief cannot be obtained unless inordinately high therapeutic doses are consumed, as for instance, one of our patients who ingests about 240 Gm. (two teacups) of brewer's yeast a day and who insists that unless this amount is taken, marked asthenia and mental depression occur.

Large doses of thiamin, riboflavin and nicotinic acid produce certain toxic effects which vary among individuals. Although 50 mg. of nicotinic acid is considered by some investigators to be a minimum daily requirement in health, this amount, if taken in a single dose, will produce in most persons the temporary symptoms of burning sensations and visible flushing of the skin. It is curious and possibly of some significance that these manifestations of overdosage resemble in some respects the chronic skin lesions of nicotinic acid deficiency (pellagra). Abels, of Memorial Hospital, in an unpublished experiment has found that daily doses of 100 mg. of thiamin (100 times the normal requirement) produce nervousness, irritability and insomnia. In this case also, the symptoms of overdosage and underdosage appear to be similar.

At one time during the progress of these clinical investigations we administered riboflavin in excessive doses (20 mg. daily) to several patients. While this quantity produced little improvement in the mucous membrane lesions of the avitaminosis, all patients suffered from such toxic effects as dimness of vision, burning of the eyelids and conjunctivae, frontal headache and some anorexia. On the other hand, moder-

ate overdosage (about five to ten times the minimal requirement in health) rarely produces any toxic effects, and from the practical standpoint is advisable when natural concentrates are used to supplement the diet.

At the present time it is difficult to explain adequately the necessity for, and the beneficial action of such high doses (five to ten times normal) of the known components of the B complex when taken in the form of the natural concentrates, namely, liver and yeast. One reasonable explanation might be the existence of essential but unidentified fractions occurring in comparatively small quantities in the natural concentrates. In any case, the requirements of individual patients either for the synthetic commercial combinations or for the natural concentrates can be determined only by therapeutic test.

The basic treatment for avitaminosis B, as for any deficiency disease, should be to supply as much as possible of the inadequate element in the form of natural foods. The patient should be directed to take at least twice daily, generous servings of green vegetables (peas, string beans, lettuce, asparagus, broccoli, etc.) properly cooked, that is, preferably steamed in a pressure cooker for a short time with a minimum of water, and conserving the juices. For patients who require a soft or liquid diet, sometimes taken through nasal feeding tubes, the vegetables after the same careful cooking can be pureed.

It is doubtful whether the quantities of glandular meats such as liver and kidney can ever be increased in the diet of the average person, so as to make any significant difference in the vitamin intake because these foods tend to become distasteful if eaten too often. For this reason it is more practical to stress the ingestion of several high vitamin B foods such as the legumes, pork, and the whole wheats rather than a single excellent source of the vitamin which is likely to prove loathsome to the patient after a short time.

The modification of an inadequate diet cannot always be depended upon completely to relieve the symptoms of a severe deficiency, and it is usually necessary or at least expeditious to supplement the diet with natural concentrates and occasionally with specially prepared combinations of the more important B fractions. A number of such preparations have been put up in the form of tablets or solutions for both oral and parenteral administration. In cases of marked deficiency, the doses should be purposely high even to the point of tolerance.

In some instances the administration of a single fraction of the vitamin B complex (thiamin, riboflavin, nicotinic acid, etc.) may cause marked improvement, but combinations of the known fractions almost always give better results. In general, the maximum benefit is obtained through use of such natural concentrates as yeast and liver. This fact, noted also by Elsom<sup>10</sup> and others, may be explained by assuming the existence of certain essential components of the B complex not yet isolated and identified, and for that reason, impossible of inclusion in any present day synthetic preparation. The superiority of a combination of several fractions rather than a single one might also be due to an essential synergistic action of the components.\*

Although the symptoms of avitaminosis may often be relieved completely by proper diet and vitamin therapy, life-long supervision of the patient's diet, sometimes with vitamin concentrate supplements, will be required. The necessity for the prolonged use of vitamin concentrates makes the expensive synthetic commercial preparations unsatisfactory for the average patient,

\* It is also undoubtedly of significance that a daily dose of 45 Gm of yeast provides about 40 Gm of available protein. According to Best,<sup>2</sup> these proteins contain such sulfur-amino-acids as methionine, cysteine and choline. These three substances increase the capacity of the organism to utilize proteins and fats. If there is an associated fatty infiltration of the liver due to a B deficient diet, the sulfur-amino-acids and choline, if ingested in sufficient quantities, will act as lipotropic agents. When the liver has been depleted of excess fats by their action, the efficiency of this organ is increased.

who will tend to discontinue treatment and suffer relapse rather than endure the financial burden imposed upon him by such therapy. We, as well as others, have found liver extract powders and solutions about as effective as yeast in the treatment of vitamin B deficiency. As Elvehjem<sup>11</sup> has stated, it is probable that liver contains all the factors of the B complex. The objection to liver is that it is both unpalatable and fairly expensive. Powdered liver extract in doses of 12 Gm. (three teaspoonfuls) daily will cost between three and four dollars a week.

Brewer's yeast is probably the most satisfactory and best all-round natural B concentrate. This substance is available in a number of forms such as dried granular solid, pastes, compressed cakes and tablets. All of these crude forms are satisfactory with the possible exception of the compressed tablets which almost always mislead patients and even physicians into an unwarranted confidence in their strength and therefore to underdosage. The potency of liquid extracts of yeast is uncertain, since the residue discarded in their preparation probably contains essential vitamin fractions.

In our experience one of the most satisfactory yeast preparations, from the standpoints of potency, cost and palatability, is granular dried yeast. When taken in doses of 30 to 45 Gm. (two to three tablespoonfuls) daily, the cost is not more than one dollar a week. Paste forms of yeast are usually several times more expensive and less palatable to the average person. Both the taste and the odor of dried granular yeast are repugnant to some patients, and in a few, therapeutic doses cause indigestion flatulence, diarrhea and even nausea. For these individuals it is best to try some other form of yeast or to substitute powdered liver extract or one of the commercial synthetic combinations for mouth or parenteral administration. If 45 Gm. (three tablespoonfuls) causes any distress, the dose should be reduced by one-third or one-half. It is of significance that many persons

do not distinguish between tablespoons and dessert spoons and also that there is considerable disagreement as to what constitutes a heaping spoonful. As a result of such discrepancies, the quantity can only be approximately estimated.

The least disagreeable method of taking the granular yeast is to place it dry in the mouth and then wash it down with a beverage. It may also be taken with a mouthful of chewed food and washed down. Some patients prefer to spread it on cereal or bread or to mix it with orange or tomato juice. For those patients on a liquid diet or for those fed through nasal tubes the granular yeast, yeast paste or powdered liver extract should be dissolved in warm water and then added to the feeding.

Some patients prefer the ordinary compressed yeast cakes sold in grocery stores for household purposes (baking, etc.). Six cakes a day corresponds approximately to three tablespoonfuls of the dried granular brewer's yeast, and while equally effective, the yeast cakes will be somewhat more expensive than the dried granular form.

*The Response of Precancerous Stomatitis to Vitamin B Therapy.* The clinical course of the mouth lesions of avitaminosis B under specific therapy is not uniform. In some instances the local and general symptoms are entirely relieved and the mucous membrane of the mouth returns to normal. In others there may be a marked improvement in the local and general symptoms with permanent disappearance of acute inflammation, healing of ulcers, relief of pain, etc., but with the persistence of papillary atrophy or hypertrophy and leukoplakia. In a few instances after an initial improvement in both local and general symptoms on vitamin therapy, even though the remedial dosage is continued or increased, there may begin after a period of one or two years, a recurrence of the signs of avitaminosis. In some cases these symptoms cannot be relieved by vitamin therapy, although unusual increases in dosage may tend to slow down the progress of the disorder.

Under vitamin B therapy, the acute mucous membrane lesions of avitaminosis B (inflammation, ulceration, pain, tender-

changes in the mouth, particularly in the tongue, will return to normal depends upon the extent and duration of such changes.



FIG. 9. M. F., female, now aged sixty-three, has been observed at Memorial Hospital for twenty years because of "sore tongue." In 1921, the tongue was described as "geographic." In 1939, the patient returned after an absence of over a year because of an increase of the soreness of the tongue and fissures at the angles of the mouth. *a*, At that time it was discovered that she had been living on a diet of white bread, butter and tea for over ten years. She was also suffering from pernicious anemia. The patient was somewhat irregular in her visits and unco-operative with treatment for over a year during which there was some improvement in the tongue. She was finally induced to take yeast and intramuscular liver extract regularly, following which treatment the perleche healed and the scrotal appearance of the tongue practically disappeared, with partial regrowth of the papillae *b*, and with marked improvement in the blood count, which returned to normal.

ness) will usually disappear or at least improve. During treatment for cancer the subjective symptoms of acute local radiation reactions are also less distressing if provision is made for adequate B intake. In patients with mouth cancer, such associated symptoms as anorexia, indigestion, constipation, nervousness, mental depression and insomnia all tend to subside or even to be eliminated completely when such precautions are taken. If the patient is markedly undernourished, there will almost always be a gain in weight. In the present series the average increase among those who gained any weight at all was twenty-five pounds, the greatest gain in any individual being thirty-nine pounds. The benefit to the patient with cancer undergoing aggressive treatment, of such an improvement in the general health, needs no further emphasis.

In precancerous stomatitis of avitaminosis B, the degree to which the degenerative

(Fig. 9.) We have mentioned that the papillae will not regenerate when atrophy has progressed to the point where the mucosa of the dorsum of the tongue resembles that of the cheek. When the atrophy is moderate or when the deficiency is acute and of short duration, there is often a prompt return to the normal state. In brief, when the stomatitis of avitaminosis B has been present for a long time, the degenerative changes in the oral mucous membranes are not reversible but will remain permanently, even though the dietary deficiency has been corrected.

#### VITAMIN B AS A SUPPLEMENT IN THE TREATMENT OF INTRA-ORAL CANCER

Supplementary vitamin B therapy should be a part of the routine during the treatment of all patients with mouth cancer. It should be the purpose to effect at least a slight gain in weight during the first one or two months of treatment, especially during

radiation therapy. Such a weight gain (marked in those who are admitted with severe malnutrition, and moderate in those who appear to be of average nutrition) is one of the most important means of building up a reserve of resistance to the debilitating effects of the necessarily aggressive treatment, either radiologic or surgical.

The diet of these patients must be closely supervised and directed. In chronic alcoholics the alcohol consumption should be radically decreased if not eliminated entirely. The caloric intake should be 3,000 to 3,500 calories a day if possible. Stress should be placed on the use of leafy green vegetables and other foods which have a high vitamin content. If the diet must be soft or liquid, as in tube feedings, these vegetables must be pureed.

Finally and of equal importance, supplementary natural concentrates of vitamin B should be prescribed. As we have already noted, from the standpoint of efficiency and cost, the most practical are the crude preparations of yeast. If these preparations cannot be tolerated, the more expensive yeast pastes or liver extract powders may be used perorally, and if these, too, are objectionable, one of the synthetic concentrates (combinations of thiamin, riboflavin, etc.) should be employed. If the peroral route cannot be used, the liver concentrates or the synthetic preparations should be given parenterally. No patient with intra-oral cancer should be subjected to radiation or to a major surgical procedure without the benefit of vitamin therapy.

#### SIGNIFICANCE OF PROPER DIET IN THE PROPHYLAXIS OF CANCER

Since it is impossible to demonstrate conclusively the existence of vitamin B deficiencies except by therapeutic tests, one can only say that such deficiencies play an important part in the production of irritative, and hence precancerous lesions of the mouth. Nevertheless, the clinician who, in the treatment of intra-oral cancer and

precancer, takes the trouble to prescribe routinely vitamin B therapy, and who observes the clinical response, can have little doubt as to the significance of avitaminosis B in the etiology of malignant tumors of the mouth. If the clinician will also note the condition of the oral mucous membranes in apparently healthy normal persons, he will be impressed by the prevalence among the entire population of the local and general symptoms of mild to severe vitamin B deficiencies.

If one accepts the postulate that the degenerative changes in the oral mucous membranes which result from avitaminosis B are important precancerous lesions, it is reasonable to believe that similar lesions from the same cause are frequently associated and of significance in cancer of the entire gastrointestinal tract (which comprises more than half of all human cancer). These theories, if sound, may have wide practical importance in the prophylaxis of gastrointestinal cancer, but there are certain obstacles in the way of their general acceptance by the medical profession, public health authorities and the lay public. It would be easier to impress both physicians and the laity if it could be maintained that there is one sole cause for cancer and precancer, and that there is one simple remedy which, taken in pill form, so many times a day for a few weeks, would effect a lasting cure and a preventative of the basic abnormality. In order to relieve avitaminosis B, however, the mode of life must be permanently modified, that is, the intake of vitamins must be increased and maintained as long as the patient lives. Such a permanent régime will, in many cases, become tedious since it is not supported by the emotional stimulus which accompanies a shorter, more intense course of therapy.

The recent widespread publicity concerning vitamins has undoubtedly been beneficial in that it has made both the profession and the laity vitamin conscious. It is difficult, however, for the average layman to interpret correctly the significance of such scientific information even though it

may be presented to him purposely in the simplest terms. At the present time vitamins are of considerable public interest which unfortunately is probably transient. In order appreciably to affect the general health by an increased vitamin intake, the hygienic dietary measures must be made the responsibility of the individual, for it is obvious that no significant number of individual diets can come under the personal direction and supervision of a physician. Furthermore, the remedy, in order to be popular, must be pleasant, inexpensive, and convenient; and the average layman, if left to his own resources, is likely to be misled into a dependence on the most expeditious though inadequate measures. As for instance, in the advertising of certain foods it is implied that deficiencies can be readily overcome by reinforcing the vitamin content of bread and cereals. In reality, since these foods do not make up a major portion of the average diet, there can be little benefit from such vitamin supplements unless inordinate quantities are consumed.

In the last few years the number of synthetic vitamin preparations which have been placed on the market has been so great as to cause considerable confusion. It is difficult and even impossible for the average physician to evaluate the merits of all of these different concentrates, most of which, although convenient, are expensive and lack some of the essential fractions of the B complex. Some drug firms have put up dried yeast in tablets containing about .6 Gm. (10 gr.) each; and whether or not specific directions are given, the average patient will assume that two or three a day (a common dose for many kinds of pills) are adequate, when as a matter of fact, it would require about seventy such tablets to supply the equivalent of 45 Gm. (three tablespoonfuls) of dried granular brewer's yeast.

It is doubtful whether the problem of avitaminosis in the general public can ever be solved by the increased sale and consumption of vitamin concentrates in any

form. Such substances find their main practical value in the treatment, under medical supervision, of aggravated cases of deficiency diseases. It is also unlikely that any large scale benefit can be derived from the reinforcement of a few food substances such as bread and cereals with such thermostable fractions as riboflavin, or by the addition of any of the known fractions to milk.

The most satisfactory source of vitamins is in natural foods, and at least a partial solution of the problem would be to increase by propaganda and public health education the general consumption of green vegetables, fresh or canned, and fresh fruits and milk. Russin<sup>33</sup> lays particular stress on the importance of adequate diets rather than reliance on vitamin supplements. Efforts should also be made to improve methods of canning and cooking so as to preserve as much as possible of the natural vitamin content. Such a program would be helped if some means could be devised to decrease the use of sweets and desserts so that it would be necessary to obtain nourishment from other foods which are better sources of vitamins.

The only really effective method of attaining such an end would probably be by indirection, that is, propaganda designed to increase the consumption of vitamin-rich foods without laying any particular stress on the special benefits to be derived. It has been demonstrated in the past in the field of commercial advertising that such an increase or modification of dietary habits can be brought about by persistent advertising of certain foods and fruits.

It is of interest to note in passing that in the present day draft army there is an average gain in weight of several pounds, indicating that in general, the draftees had been on improper diets before their induction into the army. The most obvious explanation of this phenomenon is the assumption that the weight gain was due to an increased caloric intake. On the other hand, more careful consideration would suggest that the gain may have been

due in greater part to the fact that the army diet has corrected previous vitamin deficiencies.

The B complex is, of course, not the only essential vitamin group, but at this time and in this country it is probable that avitaminosis B is responsible for more ill-health than a deficiency in any other vitamin. If the prevalence of this deficiency could be reduced, it is reasonable to expect an improvement in the general health of the population, and a reduction in the incidence of gastrointestinal cancer and also certain forms of psychoneuroses, and in the final analysis, produce a salutary effect upon mass psychology and socio-political trends.

#### SUMMARY

The degenerative changes which occur in the oral mucous membranes as the result of avitaminosis B are discussed as to their etiology, symptomatology and treatment. The clinical material upon which this study is based is drawn from the general admissions to the Head and Neck Clinic of the Memorial Hospital and includes three special series in which dietary surveys were made. The significance of the mouth lesions of avitaminosis B is discussed from the standpoints of prophylaxis and treatment of mouth cancer.

#### CONCLUSIONS

1. Degenerative mucous membrane changes are found in the majority of cases of mouth cancer. These degenerative changes are usually the result of a combination of several forms of chronic irritation (tobacco, syphilis, sepsis, avitaminosis).

2. The most frequent and probably the most important form of chronic irritation, from the standpoint of cancerogenesis in the oral mucous membranes, is that of avitaminosis B.

3. Most patients with mouth cancer already are suffering from a mild to marked avitaminosis B on admission. This disorder tends to be aggravated by the necessarily

restricted diet during the painful stages of mouth cancer. Supplementary vitamin therapy is one of the most important factors in the successful treatment of intra-oral cancer.

4. There is considerable clinical evidence that the mucous membrane lesions of avitaminosis B are not confined to the mouth cavity alone, but affect the whole gastrointestinal tract. It is therefore possible that such degenerative changes are of significance in the etiology of gastric and intestinal cancer as well as mouth cancer. It is reasonable to believe that one of the most effective means of prophylaxis against mouth cancer would be to increase the general intake of vitamin B in foods.

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# MILITARY BURNS

## AN ANALYSIS OF 308 CASES

MAJOR LOUIS F. KNOEPP, M.C.

Assistant Chief, Surgical Service, Station Hospital

FORT BENNING, GEORGIA

THE present day management of burns has been the result of many painstaking contributions in the last two decades. Until 1925, most burns were treated with expectancy and a patient with 40 per cent of body surface involved was given a generally hopeless prognosis. Most deaths had been ascribed to primary and secondary shock associated with the elaboration of some toxin at the burn site. In that year Davidson proposed his epoch-making tanning method which appealed more from simplicity in handling the patient. The general improvement in mortality figures from this type of therapy stimulated further investigation.

In 1930, Underhill showed startling relationships between the hematocrit concentration and mortality. In dogs who had as much as 20 per cent body surface burned, there was a universal rise of hemoglobin and red cells with a loss of as much as 70 per cent of body plasma into the tissues. The loss of plasma through increased capillary permeability was irreversible and had to be compensated by the intravenous administration of large amounts of fluids. Plasma chlorides were also rapidly depleted and Coller and Maddock advocated giving 0.5 mg. of sodium chloride per kilogram of body weight for each 100 mg. lost beneath the normal blood level of 560 mg. per cent. The recent advances in preparation of plasma and its use have been most effective in creating a normal protein balance and hematocrit percentage. Harkins developed a formula for administering plasma in that 100 cc. were given for each point of rise of the hematocrit over the normal of 45.

As early as 1933, Aldrich and Firor had challenged the toxemia theory. They

claimed that, aside from initial shock, patients died from purely infection and sepsis. This evidence was based on numerous cultures taken from the burn site before and after application of the tanning agent, and revealed heavy cultures of hemolytic and nonhemolytic staphylococci and streptococci. They proposed careful débridement to the point of wound sterility before applying the tannic acid. Moreover, various dyes were proposed as gentian violet and later a triple dye composed of gentian violet, brilliant green and acriflavine to promote bactericidal action against any remaining organisms. Other investigators with the same mode of attack, proposed continuous wet dressing with azochloramid and applications of silver nitrate by either solution or stick. These methods were advocated alone or in combination with the tannic acid method, and frequently modifying both with the resumption of the time-worn ointment forms of therapy.

The availability of blood plasma for early treatment of shock, the careful débridement of the burn, and the development of the sulfonamides stand foremost in attaining our present-day results. The first consideration for any burned patient is for his life. Blood pressure readings are taken frequently, red cell and hemoglobin estimations are made, and the patient is given sufficient plasma to convert the hematocrit percentage to normal. Fluids and morphine are prescribed in adequate amounts until all evidence of shock is controlled. Most patients regardless of the degree or extent of the burn will respond to this treatment within three or four hours, and those who do not, will probably not respond to any form of therapy. In the

favorable group, the burn is then débrided thoroughly with aseptic technie. Green soap and water are used until the surgeon is satisfied that all foreign particles are removed. All necrotic tissue and vesicles are excised and the burn is lavaged with sterile water or saline. This débridement may require heavy doses of opiate to control pain, and it is believed that an adequate cleansing can be done with sterile gauze without resorting to the scrub brush. The latter instrument would appear to increase the amount of nonviable tissue and traumatize sufficiently to affect after-healing. Gentleness will in a good many cases of shock, mark the difference between a survival or death.

After thorough cleansing the burn is ready for one of the tanning agents. It is not believed that the end result is influenced by the agent chosen, and all forms have been used in this series with equal success. There is an apparent advantage in a 1 per cent aqueous solution of gentian violet, in that two or three applications usually suffice to provide a good crust. Ointments as boric unguentum, amertan, or gentian jelly are used on the face and fingers. Sterile mineral oil is dropped into the eyes and ears as long as there is swelling of surrounding tissues. The burned areas are then encased in sterile gauze for forty-eight hours until the crust gives sufficient protection alone. Motion of all joint surfaces is encouraged as soon as swelling has subsided, usually after forty-eight hours, and full range of motion is attained daily. This prevents contracture, promotes flexibility of the crust, and has not, in our hands, delayed wound healing.

In burns which are treated after twenty-four hours without proper débridement, or in those who present temperature elevation after seventy-two hours, a search is made for a focus of suppuration. If found, the overlying crust is removed and the part encased in continuous wet boric acid or saline dressings until all evidence of infection is absent. No attempt is made to reapply a tanning agent over previously

septic areas as experience has shown that suppuration will reoccur. Ointments, on the other hand, are chosen and such dressings are changed daily, washing all ointment from the burn before applying it fresh. If no focus of infection is found, sulfathiazole is given orally in full therapeutic amounts to obtain a blood concentration of the drug of 5 or 6 mg. per cent. If suppuration exists, it will eventually become evident and may be then handled as previously advocated.

TABLE I  
CAUSES OF BURNS

	No.		No.
Gasoline.....	89	Lysol.....	13
Flame.....	47	Iodine.....	12
Hot water.....	41	Lye.....	12
Hot stove.....	19	Phosphorus.....	8
Hot ashes.....	11	HgCl <sub>2</sub> .....	3
Hot metal.....	5	Cresol.....	3
Hot grease.....	5	Phenol.....	3
Hot water bag.....	3	Ammonia.....	2
Steam.....	3	H <sub>2</sub> SO <sub>4</sub> .....	1
Gunpowder.....	11	Gasoline.....	1
Hot tar.....	2	KMnO <sub>4</sub> .....	1
Electric.....	1	SO <sub>3</sub> .....	1
Sunburn.....	8	CO <sub>2</sub> snow.....	1
Ultraviolet.....	1	Gunpowder.....	1
Total thermal.....	246	Total chemical.....	62

If at the end of ten days the crust has not shown separation, wet dressings are applied to loosen it. In third degree burns, skin grafts are then applied to the granulation tissue base after complete removal of the crust. These have been either Davis pineh grafts or split-thickness grafts for joint surfaces. The usual pressure dressing is applied following the graft.

This analysis comprises a study of 308 patients admitted to the Station Hospital, Fort Benning, Georgia from January, 1927, to December, 1941. During this interval there were approximately 95,000 hospital admissions, burns representing a ratio of 1 to 300. All were male patients with the exception of one female child. The average age was 24.2 years with 93 per cent falling in the eighteen to thirty-five-age group. There were 266 white and forty-two colored patients, and twenty were considered mild enough to be treated as out-patients.

Table I shows the general causes of these military burns. Of the total, sixty-two were chemical and 246 thermal. Included in the latter are nine cases of actinic origin. Gasoline leads in order of occurrence as most of the vehicles and field apparatus are fueled with this commodity. The importance of this agent has increased steadily in the past few years. Actual flame contact is distinguished from gasoline burns inasmuch as the chemical factor of the fuel is not present. Most of the patients received flame burns in an attempt to extinguish a blaze, or from the explosion of some inflammable gas. This type of burn is distinguished again from contact with a hot object or hot material, as hot grease, tar and gunpowder, which may afford more prolonged and intense heat from their contact with the tissues. In the main, agents are important only as their chemical or thermal action is implied.

TABLE II  
COMPLICATIONS

	No.	No.	
Pneumonia.....	2	Corneal opacity.....	2
Cicatrix, painful.....	1	Shock,* severe.....	6
Symblepheron .....	1	Shock, moderate.....	23
Anuria*.....	1		
Nephritis, acute.....	1		

\* Died.

The criteria for study of any burn management can be derived from the collection of the following data: mortality rate, complications and the length of stay in the hospital. The type and seriousness of burns in any series of cases will materially affect the mortality rate. Military burns on the whole are potentially serious but most of the patients are seen promptly by some medical attendant. Moreover, many burns of minor character are hospitalized which in civilian life would not be seen. These features have led to a strikingly low mortality rate of 1.3 per cent in the group. There were, in addition to the four deaths reported, four others who were dead before admission to the hospital. With the exception of one case, all patients involved in fatal cases died within twelve hours due to the extent of the burn, despite intensive

shock treatment. The other patient died on the eighth day of total anuria secondary to sulfathiazole administration.

There were few complications as can be seen by Table II, and particular attention is called to the paucity of contractures. This, it is believed, can be attributed almost entirely to careful débridement and enforcement of early active and passive motion. Pneumonia, a fairly common complication in most lists, occurred but twice due to promptness in allaying any threat of the infection by the use of the sulfa drugs. Shock in varying degrees was

TABLE III  
PERCENTAGE AREA OF BURNS

All Burns	Area, Per Cent	No.	Hospital Stay, Days
1 or less	18	13.1	
2 to 5	15.5	18.0	
6 to 10	41	24.2	
11 to 15	15	20.2	
16 to 20	10	38.7	
21 to 30	4	37.2	
31 to 40	2	75.5	
Over 40	4	3.7—all died	
Special burns			
Penis and genitalia...	0.5	21	21.5
Actinic.....	33.3	9	6.3

present in most of the patients with 20 per cent or more of surface involved, but it was not credited for analysis unless it was present in the secondary or hemagenic form. Other complications which may develop were not present in this series. Septicemia is one of the most common complication and may lead to metastatic abscess formation elsewhere. Tetanus has been reported by Newberger in a number of patients, but most recent series do not show it. All of these patients received either a protective dose of antitetanic serum or a stimulating dose of tetanus toxoid on admission. Duodenal ulcer as described by Curling has been reported as fairly frequent by Pack and Davis. Occasional instances of carcinoma developing in

the burn scar (Marjolin's ulcer) have been reported.

The length of stay runs parallel with the healing of the burn and it is an important measure for effectiveness of treatment. It is dependent upon (1) degree of the burn, (2) extent of the burn, (3) location of the

this region comprises at most 0.5 per cent of surface area, the length of stay was equal or greater than the average burn of the body, regardless of the latter's extent. That there is a distinct difference in healing time of chemical and thermal burns can be seen from Table IV. Here the average

TABLE IV  
DEGREE OF BURNS

	Degree	No.	Hospital Stay, Days
All burns			
308 cases.....	1st	114	11.8
374 burns.....	2nd	229	21.4
	3rd	31	49.9
Chemical			
62 cases.....	1st	28	
68 burns.....	2nd	32	16.1
	3rd	8	average

burn, (4) type of agent, (5) concomittant injuries, (6) presence of infection and (7) treatment.

Most of these burns involved 5 per cent or less of body surface. Berkow's method of estimating surface area involved was utilized in Table III. There was little difference in hospital stay when the burn involved 5 or 15 per cent. Above this figure, hospital stay was remarkably prolonged. The aver-

TABLE V  
REGIONS OF BODY BURNED

Hands.....	91	Chest.....	31
Legs.....	90	Feet.....	28
Forearms.....	67	Genitalia.....	27
Head and neck.....	64	Eyes.....	21
Thighs.....	40	Abdomen.....	20
Arms.....	34	Buttocks.....	11

age duration of treatment for all burns was 20.5 days. The degree of the burn varied directly with the time of healing and third degree burns required twice the time as second degree burns as can be seen from Table IV. The regions of the body burned were the hands, legs, forearms, head and neck, thighs, arms, chest, feet, genitalia, eyes, abdomen and buttocks in the order named. (Table V.) There is a distinct difference in healing time in burns of the genitalia as compared with other regions. While

TABLE VI  
INFECTED BURNS

Days elapsed before seen.....	0	1	2	3	over 3
No. of patients.....	37	13	5	6	10
Total infected.....	71				
Percentage.....	23				

Degree	No.	Hospital Stay, Days
1st	0	
2nd	67	26.1
3rd	15	50.4

hospital stay for chemical burns was 16.1 days while the average for the whole group was 20.5 days. This is all the more impressive by the fact that chemical burns had an average degree of 1.67 while thermal burns had an average of 1.43.

The occurrence of infection delays the healing of burns in general. No first degree burns were found to be secondarily infected but the hospital stay for second degree

TABLE VII  
INFECTED BURNS

Day after admission when infection developed.....	1	2	3	4	5
No. of patients.....	36	22	8	2	2
Duration of infection.....	Under 5 days	Over 5 days	Over 30 days		
No. of patients.....	51	20	1		
Average 4.1 days					

infected burns was 26.1 days and of third degree infected burns 50.4 days. There were a total of seventy-one secondarily infected cases or 23 per cent of the entire group. Of these, thirty-seven were seen promptly on the day when the burn was incurred. That delayed treatment may be a factor in occurrence of infection may be seen from the fact that thirteen patients were seen after twenty-four hours, five after forty-eight hours, six after seventy-

two hours, and ten after three days or more. All infections were present either at the time of admission or developed by the fifth day as shown in Table VII. Of all the infected cases, fifty-one remained septic for five days or less, and only twenty remained septic longer. One patient remained infected for thirty days, but the average duration of infection was only 4.1 days.

Four of the third degree burns were skin grafted. This did not affect the hospital stay in these patients, but it did modify the cosmetic and functional results, as all were deep burns over joint surfaces. All of these grafts were performed since 1939, therefore, the percentage is not a true estimate of the number of patients deserving this form of treatment.

#### CONCLUSIONS

1. The present-day management of burns depends on prompt use of blood plasma for shock, careful débridement of the burn and the use of the sulfonamides in curbing infection. Early active and passive motion is encouraged in all patients.

2. A series of 308 military burns is analyzed occurring over a period of four-

teen years, with a statistical evaluation of factors determining the results of healing.

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35-26

# INITIAL TREATMENT OF TRAUMATIC WOUNDS

LIEUT. COL. JOHN L. GALLAGHER, M.C.

Post Surgeon and Senior Flight Surgeon, Station Hospital

STOCKTON, CALIFORNIA

IT is believed that a person receiving traumatic wounds in this day of modern surgical achievement should have the full benefit of a plastic repair promptly done under proper conditions by a surgeon capable of obtaining a minimum of deformity and disfigurement for his patients.

If such wounds are properly treated within a reasonable time of their incurrence, recovery will be hastened and the hazard to life from infection will be reduced. Deformity, disfigurement and blemishes while awaiting secondary plastic repair will be avoided. The pain, inconvenience, loss of time and expense of a second operation or a series of them will be averted. In case of injuries so complicated and extensive that secondary plastic operation is unavoidable, future surgery will be enhanced and a good final result will be assured.

Where immediately available, a capable plastic surgeon should be called to attend traumatic wounds likely to result in deformity or disfigurement. However, appreciable delay precludes a satisfactory end result and is dangerous to the life of the patient; hence every surgeon should become proficient in the repair of such wounds so as to leave the minimum of scar and distortion. He should preserve tissues readily available for secondary repair and use every judgment to avoid the need for additional surgery.

In the repair of wounds it is necessary for the surgeon to study them carefully in order to determine the anatomical disarrangement and the nature of the instrument causing the injury, as well as the complications likely to ensue. Proper records of all injuries should be kept as to how, when and where they were sustained. It therefore becomes obvious that a work-

ing classification of wounds must be adhered to. The following simple grouping is suggested:

1. Abrasions: mild, moderate or severe; small areas to extensive areas.
2. Wounds: incised, mild, moderate or severe.
3. Wounds: lacerated, mild, moderate or severe.
4. Wounds: contused, mild, moderate or severe.
5. Complications or variations of the above: penetrating certain areas, perforating others, amputating a member, dividing a lip, an ear, the tongue, an eyelid, nerves, arteries, tendons, evulsing a cartilage, a nail, etc.

Traumatic wounds about the face, head, arms, hands and feet are generally not given the degree of respect due them. An attempt is made for closure without the proper setting and without sufficient armamentarium to accomplish a proper operation. So often a wound looks innocent enough by observation and its full extent is not realized until its repair is in process and an adequate exploration reveals astounding complications. For instance, an apparent moderate scalp wound may very likely extend into a depressed fracture of the skull and in turn may have a foreign body penetrating the brain. (Such a case actually happened on this service recently.) Furthermore, such an innocent looking wound may be complicated by the division of important nerves or tendons.

Since the above is true and infection generally is so disastrous to all wounds, the following rules are recommended and are actually enforced at this hospital:

Any wound requiring sutures should be treated with the same respect as would be a major abdominal procedure so far as

aseptic set-up goes. If upon admission the patient's wounds are dressed and some information is available as to the nature of

The surgeon who is to cleanse the wounds puts on sterile gloves, and follows the procedure outlined below; the others get



FIG. 1. Taken approximately one hour after patient was seriously injured in an automobile crash. Preoperative cleansing has been only partially accomplished. The ragged wound dividing lower lip extends to bone from left lower cupid tooth to inferior border of mandible avulsing the soft tissues covering the mandible from the angle to the symphysis menti tearing the floor of the vestibule. The wounds of the upper lip and nose perforate into their respective cavities.



FIG. 2. Preoperative cleansing is practically complete. The tissue hook holds up the left portion of the lower lip.

the wound, the dressing should not be disturbed until the operative procedure is in progress. Under no circumstances is a dressing to be removed outside of the surgical clinic, and there only after the surgeon has scrubbed his hands and covered his head with skull cap and mask. No person is to enter the operating room without having on cap, mask and gown, while the operation is being prepared for or is in progress. The surgeon and his assistants undergo the same preparation as for a major operation, donning operating pajamas, cap, and mask, afterward completing a full surgical scrub.

into sterile gowns and gloves and await the actual start of the operation. After an unsterile nurse or attendant cuts the bandages free, the entire wound area, including the wound, is cleansed of all dry blood with hydrogen peroxide solution. Any necessary shaving is done with a sterile razor, followed by a thorough washing of the entire area with sterile whipped white soap which is lavaged away with sterile water; the sponges used are held with the forceps throughout. The area is then dried and thoroughly cleansed with ether, and the skin antiseptic is applied to the entire area up to the wound edges. The surgeon now removes his gloves, and if indicated goes through the scrub procedure again, gets into sterile gown and gloves and the operation is ready to proceed. The patient is draped to expose with ease all wounds to be treated, and all except the first one are temporarily covered.

At this hospital 2 per cent procaine as local, or combined with nerve block, is used sparingly as the anesthesia of choice in the

The repair of the wound is influenced by the extent of the damage, the degree of contamination, the time intervening since

FIG. 3.



FIG. 4



FIG. 5.



**FIG. 3** Preoperative cleansing is complete, skin antiseptic has been applied and the wound has been draped

**FIG. 4** Surgery has been completed except for retention dressing

**FIG. 5.** Seven days after primary surgery; all external sutures have been out for four days, the wound being held in close abutment with the collodion strips, which were reapplied for four additional days.

primary closure of traumatic wounds, and is done prior to the actual cleansing and exploration of the wound. The wound is now inspected and thoroughly searched for foreign bodies. If there is clotted blood and foreign matter such as dirt, glass, pieces of clothing, splinters of wood or hair present, such are removed; the instruments thus used are discarded, and the wound is lavaged with peroxide followed by irrigation with sterile saline until clean. The soiled drapes are discarded, the skin antiseptic is re-applied up to and including the skin edges, and new drapes are placed. If there is a tourniquet, it is now released and the necessary hemostasis is performed, the small grasps taken with mosquito forceps. The wound is thoroughly explored and a decision is reached as to how it will be repaired.

the injury and the demands of the situation. For instance, in the case of an ear almost completely excised, an extensive effort must be made to re-unite it so long as there is any evidence of viability. The longer the intervening time since injury, the simpler and more cautious the repair should be. A grossly contaminated wound indicates caution and minimal procedure, yet one must endeavor to obtain the minimal formation of cicatricial tissue, disfigurement and deformity.

The actual appearance of the wound influences the degree of surgery that may be undertaken. If the wound has had good first-aid care, for instance if a sterile pressure bandage has been used, it may reach the surgeon several hours after the injury and still be free of edema and weeping angry edges. On the other hand, a wound

may present an unfavorable appearance in a short time if proper first-aid care has not been given. (Figs. 1 to 5.)

*Aims of Operation.* The aims are: (1) To re-establish anatomical relations and restore the features as nearly as possible to their original appearance; (2) to use methods that will give universally good results, doing scanty débridement where indicated to avoid the complication of infection; (3) to prepare and close the deeper structures so that equalization can be obtained in closing the skin and (4) to close the skin in such a manner that the resulting scar will be of skin level or slightly higher when all shrinkage has occurred.

A careful study of the wound edges with a magnifying glass or magnifying eye glasses will usually show slight irregularities of the edges at one or more places (notch on one side, projection on the other) left by imperfections of the sharp edge causing the wound. These irregularities will greatly aid in the exact re-approximation of the skin edges though they are usually drawn out of place by muscle pull. If a débridement of the wound edges is indicated, the above irregularities may be used in two or more ways: (1) by gentian violet lines drawn back from them and (2) by close sutures temporarily approximating the skin edges, followed by cross-marking the temporarily closed wound, and then by an excision of the indicated amount of skin, the final closure joining the cross-markings.

If a wound is in condition to be closed, it will usually withstand the necessary débridement. However, the débridement should always be as stingy as conditions will permit, eliminating shredded, devitalized muscle or dirt impregnated tissue when it can be removed without hazard to important nerves and vessels.

Hemostasis should be complete. Scant bites with small forceps are tied with very fine plain catgut or white silk. Sulfanilamide crystals are placed in grossly contaminated wounds and over the closure, and antitetanus gas gangrene prophylaxis

is given whenever indicated. At times x-ray therapy is employed prophylactically. Re-approximation of the deeper tissues requires a careful rejoicing of the structures in their proper anatomical relations, with the finest sutures practical for the tension placed upon them. Whenever a wound is in a region traversed by important nerves, function tests should be performed. If nerve function is lost, a definite effort should be made to demonstrate the severed nerves concerned and to repair them, provided, of course, that the wound is in operable condition. No. 0000 white silk on fine atrumatic needles is excellent for nerve repair. The same applies also to wounds in the area of tendons. However, if the wound shows any signs of infection or if the interval since injury is plus four hours, it is ordinarily best to leave the tendon closure for a secondary procedure.

#### GENERAL PRINCIPLES IN THE TREATMENT OF COMPLICATED WOUNDS

*Wounds Likely to Result in "Trap Door" Scars.* Incised wounds leaving the skin cut on a sloping bias are likely to result in "trap door" scars. If there is ample skin for excision of the two sloping edges without distorting the features and the wound is in good condition, it is thought advisable to excise the edges squarely. However, if such débridement of skin is not practical, the wound should be carefully closed from the deep structures out. Care is given to the subcuticular closure, and with the surgeon using numerous very fine black silk sutures, the skin is anchored all the way up the bias. A pressure dressing is sutured over the wound, and overlying this dressing a large sponge of cotton waste is placed and firmly held with stockinette bandage. Islands of skin scooped up or flaps raised with narrow, thin bases also have sloping edges. If these wounds are too large for simple excision and closure, they should be treated as outlined above and in addition the midportion should be anchored down with mattress sutures.



FIG. 6.



FIG. 7.



FIG. 8.



FIG. 9.



FIG. 10.

FIGS. 6 TO 11.



FIG. 11.

Fig. 6. Army nurse seriously injured in automobile wreck approximately seven hours prior to surgery. Photo taken twenty-four hours after surgery, showing the original dressing which consisted, from skin out, of scarlet red gauze, retention pad without sutures, forehead-nasal lead splint lined with sterile gauze, three bulky sponges of cotton waste, to which pressure is imparted by circular bandage of bias-cut stockinet. Fig. 7. Taken ten minutes after Figure 6. Gives some idea of the extent of injuries to head. The wound extending to bone from midforehead entered both nasal fossae and ended at tip of nose. The supporting structures of the nose were crushed and the soft tissues were avulsed laterally to cover eyes partially. A square em. island of superficial tissues which was scooped from the left nasal dorsum to hang by a few shreds was used as a full thickness skin graft. The wound of the medial one-third left upper lid partially divided that structure. Attention is called to the relative absence of edema, as evidenced in Figures 7, 8 and 9, taken on consecutive days with reapplication of the large pressure dressings following Figures 7 and 8. The author believes the swelling from edema would have been enormous without a pressure technic. Fig. 10. Here on the third day all sutures except the intranasal sutures and those holding the skin graft on the side of the nose are removed. The sterile tension-relieving strips are used for a triple purpose: (a) to hold the wound edges in abutment (b) to hold pressure to the skin graft, and (c) to hold the severe compound fractured nose in alignment and conformity. Fig. 11. Final result of the primary operation.

*Wounds with Opposing Edges of Unequal Length.* Wounds in which the instrument cutting the skin took a wide uneven bite, or in curving wounds having surgical débridement (the wider the débridement, the greater the disproportion), the opposing edges must be equalized as to length. This can be done by taking an equalizing triangle of skin from one or both angles of the wound. (Figs. 6 to 11.)

*Other More Difficult Wounds: Wounds with Extensive Skin Loss.* All wounds with a loss of skin too extensive for approximation require immediate skin grafting when in operable condition. At this hospital free, transplanted, thick-split skin grafts on wounds as old as eight to ten hours, having had a proper pressure dressing as first aid, have taken in approximately 100 per cent. Thereby the patient is saved the distortion from cicatricial contracture and also a prolongation of hospitalization that would result from awaiting the otherwise unopposed skin edges to granulate in and scar over with the added hazard of infection. This same technic is used to cover over a guillotine loss of a portion of a finger, tip of the nose, tab of an ear, and results in saving, in the case of fingers, the length which would be lost by flap closure or in minimizing and preventing the hard, often painful, scar that would form if allowed to granulate in and scar over.

Wounds that divide the lip, the tongue, wall or walls of the nares, the eyelid or the external ear, when fresh and in good surgical condition, require complete plastic closure. This is done with careful scanty débridement and accurate fitting of the underlying, sutures, e.g., mucous membrane, cartilage, salivary and lacrimal ducts, muscles, etc., held with simple or mattress sutures of fine white silk. Care must be exercised in rejoining the opposing mucocutaneous junctions. The subcutaneous tissue and skin closure is cared for as under *details of technic*.

In parallel wounds too close together for separate outside suturing to obtain eversion of the edges, a double bite, triple bite,

etc., of the end-on mattress suture can be used and the return sweep of the needle passed under both or all of the wounds. Each wound can then receive its interrupted suturing with the retention suture encompassing all. Triangular wounds, or wounds that cross-complicate the repair, are harder to prepare and obtain eversion in, and the blood supply in the corners is likely to be tied off in the suturing and become gangrenous if care is not taken. The blood supply is likely to be cut off at the angles by the use of subcuticular stitches if special care is not taken to keep the bites small and thin. One end-on mattress suture is well placed where the point of the angle joins its notch in triangular wounds, but two placed at right angles near it will almost certainly result in its becoming gangrenous. Here interrupted sutures very close to the edge must be used and can be so placed that the point is somewhat forced into its notch. For the corners where two wounds cross, two end-on mattress sutures opposite each other joining the four corners make a good start, but preclude the use of other end-on mattress sutures in the close vicinity. Use of interrupted sutures straight through at right angles to the level of the skin will help with the eversion and full abutment of skin edges. Otherwise the treatment is as described below.

*Details of Technic in Wound Repair.* Wounds which do not extend completely through the skin are repaired by close approximation with fine sutures. However, any wound which goes through the base of the skin so as to gape, or which can be separated to reveal subcutaneous tissue, requires detailed repair. Otherwise, the base of the skin will separate, leaving a broad, thin area of poorly epithelialized scar.

*Undercutting the Skin.* In fresh, clean wounds free of early signs of infection, a slight undercutting of the skin, with removal of a lineal wedge of the subcutaneous tissue, which would otherwise tend to prop open the wound, is of a definite advantage

to the ultimate skin healing. This permits close, easy abutment of the opposing edges.

**Subcuticular Sutures.** The subcuticular

similar sized plain catgut on a half-circle, cutting needle (atraumatic needle preferable). Again, when these sutures are tied,

FIG. 12.



FIG. 13.



FIG. 14.



FIG. 15.



FIG. 16.



FIG. 17.

For descriptive legend see page 239.

sutures should close the base of the skin. The skin must be held in equalization while they are being placed. The equalization of the skin can be obtained as before described or by the use of fine tissue hooks held at the extremities of the wound by an assistant, beginning the interrupted subcuticular suturing near one angle, placing all sutures, clamping the ends to be tied later, then tying these sutures from the extremities toward the middle alternately. Then without the hooks a suture is placed at each angle to avoid its being puckered by being held in place with the hooks. The sutures used in the subcuticular closure must be fine, No. 000 or No. 0000 white silk or

the skin is actually approximated with some eversion.

**Skin Closure.** The skin sutures require exacting care. The edges should be everted evenly with the highest eversion at the center of the wound. The sutures should be so placed that opposing edges are caught equidistant from the angles at the same depth from side to side and so placed that the entire depth of the skin is abutted for its full thickness. The sutures should actually stretch the depth of the opposing edges. The most important feature of the skin sutures is that they be placed close to the skin edge so that, if they cut, the resulting scars will not be large ones and will be

easily repairable. The sutures must be fine, of nonirritating material and not tied too tightly. It is unnecessary for the suture to

suture, the surgeon crosses the needle underneath the wound line and out at right angles to the skin at an equal distance. The



FIG. 18.



FIG. 19.



FIG. 20.



FIG. 21.



FIG. 22.



FIG. 23.

For descriptive legend see page 239.

be further away from the skin edge than the thickness of the skin in the area being repaired. Every precaution is taken to avoid adding trauma to the already injured skin.

*End-on Sutures.* The end-on mattress suture is placed through the edge of the skin and sloped to whatever degree necessary to obtain the desired amount of eversion in the wound, and out on the other edge at exactly the same depth and angle. At the back-sweep while lifting on the suture so as to stretch the skin away from its base, going through the skin at right angles just beyond the emergence of the

knot is tied without tension, no effort being made forcibly to abut the skin edges. Even though the top edge separates slightly, this suture should not be tight. In the placement of these sutures, approximately one for each one-fourth inch, the fine tissue hooks above mentioned aid in lineal equalization of the skin edges and the gentian violet equalization marks above mentioned may be used. The same caution should be taken not to hold the angles in pucker while placing the wound angle sutures.

*Interrupted Suture at Right Angle.* Interspaced midway between each end-on suture, an interrupted suture is placed

FIG. 24.



FIG. 25.



FIG. 26.



FIG. 27.

FIGS. 12 TO 27.

Illustrations showing the postoperative care following repair by modified "Poulard's" Method, of an old adherent scar in a depressed frontal fracture. This postoperative care is used routinely by the author in traumatic and many other wounds. Figs. 12 and 13. Before operation. Figs. 14 to 17. Represent a modification of a pressure technic originally suggested to author by Dr. James Barrett Brown. Fig. 14. The complete dressing. Fig. 15. The small surgical pad sutured over wound to concentrate pressure to the wound. Fig. 16. Showing the wound overlayed with scarlet red gauze. Fig. 17. Shows all external sutures and the long sponge-holding sutures. (Never tied tightly.) Fig. 18. The end-on sutures have been removed. Fig. 19. Bandage strips anchored to alternate sides with collodion. Fig. 20. Surgeon and assistant pull alternate strips and glue them down across a strip of gauze over scarlet red gauze. Fig. 21. The collodion strip ends are tagged with adhesive. Fig. 22. Pressure is added to the wound site with adhesive over folded gauze. Fig. 23. The third day dressing. All sutures are out. Fig. 24. The bandage strips are glued to the skin on alternating sides right up to the skin edge. Fig. 25. The strips have been fastened across, as above. Fig. 26 and 27. Show the after results of the one operation.

which goes through the skin at right angles and back from the wound edge on a level with the back bar of the end-on suture. This suture is tied with the knot directly on top of the wound and an effort is made to abut the skin edges without tension.

*Shallow Wound Sealing Sutures.* A third row of sutures is placed equidistant between the above two types of sutures and is of the finest available silk, No. 000 or No. 0000 black, threaded on a very fine half-curved eye needle and placed sloping very close to the surface, and to the edge of the skin. It is tied quite firmly and used to seal the outer edge. Complete coverage of the wound by skin is essential. The wound and area now are thoroughly cleansed of all dry blood with peroxide and saline.

*Retention Sutures.* The retention sutures, involving the use of size D black silk or horsehair suture on a noncutting, fine, triangular, pointed needle, one inch long, half-curved, are placed back approximately one-half inch from the skin edge where practical, and again go directly through the skin and out at right angles, being placed at about one-half inch distance lineally. These sutures are left long. (Figs. 12 to 27.)

*Dressing the Sutured Wound.* With the wound entirely cleansed of dry blood, scarlet red 5 per cent ointment impregnated in three-inch fine mesh bandage gauze is laid over the wound. Over this is placed a row of cotton waste in gauze, of sufficient thickness to hold the retention sutures from their tendency to pull toward the wound. The retention sutures are tied over this roll with caution against tying them too tight, for tension here would be disastrous. Gauze is then placed around the roll to convert the dressing into an oval pack. Then a large sponge made of cotton waste is placed over the entire area even though it may be necessary to cover one or both eyes, and a pressure bandage of diagonally cut stockinette is applied to form and hold pressure. The aim of this type of dressing is to avoid stagnation in the wound area with resultant edema

formation, and thus to aid the return circulation.

*First Change of Dressing.* The dressing is left on for twenty-four to forty-eight hours, depending upon the comfort of the patient. It is then removed carefully with saline soaking used if it is stuck to the wound. The retention sutures are cut close to the skin on one side and removed. The scarlet red dressing is soaked off with peroxide. Ordinarily, it is found that the retention sutures have served as drains for the wound as evidenced by dry blood at their points of emergence. The wound and the surrounding areas are found to be free from edema and swelling and the wound edges entirely free of dried serum or other wedge-forming material. The wound is washed with peroxide and is painted with Scott's solution which is allowed to dry. All end-on sutures are removed at this dressing if forty-eight hours have passed, or after twenty-four hours if such sutures appear to be cutting.

*Collodion Tension Relieving Strips.* A three-thickness fold of scarlet red impregnated bandage gauze is laid over the suture line, just wide enough to cover it, and over this a small strip of gauze. Using collodion as glue, sterile strips of bandage one-eighth inch wide are fastened to the skin on alternate sides crossing the wound, close to the gauze. Using a hand hair dryer to speed drying, the dressing surgeon pulls on a strip on one side with his left hand while an assistant pulls on the next strip on the opposite side with sufficient force to take all tension from the suture line. (Figs. 19 to 25.) All strips are glued into place.\* In this manner the scarlet red is held firmly to the wound edge and all tension is removed from the sutures. On top of this a firm sterile gauze dressing is placed with adhesive strips at right angles to the wound in such a manner as to reinforce the pressure in the direction of the wound edges.

\* I devised this method of relieving the wound of the normal skin tension (tendency of the wound to separate) approximately four years ago and used it since with a great deal of success.

*Second Change of Dressing.* When forty-eight to seventy-two hours have elapsed from the time of operation, this last dressing is removed. All remaining sutures are taken out and the tension-relieving collodion strips are again applied, from well back of the wound up to the very wound edge. (Figs. 24 and 25.) While alternate strips are pulled on with just sufficient force to relieve all tension from the wound, the glueing process is completed. A sterile gauze pad is laid over the wound edge, and adhesive strips are laid across the pad in the same direction, thus covering the extremes of the collodion strips. This dressing remains until the eighth postoperative day. Quite often all sutures are removed twenty-four to forty-eight hours after surgery and the tension relieving collodion strips put in place; these serve to hold the wound in approximation without untoward effect. However, where adequate pressure is held on the wound area, and undue tension is thus kept from the sutures with the strips, there is seldom inclination for the sutures to mark. Allowing them to remain for a longer interval—a total of three or four days—is believed to be safer. It is only when slight edema occurs or the patient has acne, has a very irritable skin, or has an abrasion complicating the wound, that earlier removal of the sutures seems indicated. When the sutures are found to be

too tight, they are removed and the skin is held in close approximation with the collodion strips. Even if all sutures have to be removed at the twenty-four hour dressing, the tension relieving strips hold the skin in close abutment without tension, and also tend to hold the edges level in depth, and the final result is seldom any the worse for it. I know of no other safe means of so early a total removal of external sutures. The strips are sterile and the wound is not sealed with the collodion.

#### CONCLUSIONS

1. Traumatic wounds should have immediate plastic repair in order to obtain the minimum of deformity and disfigurement.
2. For wounds likely to result in gross disfigurement a plastic surgeon, if immediately available, should be called.
3. Since delay is ruinous to the end result and dangerous to the life of the patient, every surgeon should become proficient in the initial plastic repair of traumatic wounds in order to reduce the incidence of scar formation and disfigurement.
4. Regardless of the prior contamination to the injury, the strictest asepsis is required in the surgical repair, with full protection from respiratory contamination.
5. The collodion tension-relieving strips are a definite aid in obtaining a minimal scar.



# OPERATING ROOM DEATHS\*

## A STUDY OF TWENTY-THREE CONSECUTIVE CASES IN WHICH AUTOPSIES WERE PERFORMED

FENNELL P. TURNER, M.D. AND

Department of Surgery, Royal Victoria Hospital

F. ARTHUR H. WILKINSON, M.D.

Chief Anesthetist, Royal Victoria Hospital

MONTREAL, CANADA

HERE is no experience in medicine more distressing than that of an "operating room death" and this is especially true when the death is sudden and unexpected. With this thought in mind we have studied twenty-three consecutive cases of operating room deaths in which autopsies were performed, covering a period of ten years from 1931 to 1940 in the Royal Victoria Hospital. Excluded from this series are all neurosurgical cases save one which was included because of close similarity to another case in this series. All patients were under anesthesia whether it was local, spinal or general, and all patients were either undergoing operation or had undergone operation and had not yet been returned to the ward.

In studying these cases an attempt has been made to find both the underlying and the immediate causes of death, and if possible to put them both on a physiological as well as an anatomical basis. In a limited way certain results might be obtained from such a study: (1) a better understanding of just what constitutes a definite surgical and anesthetic risk; (2) a more rational basis from which to choose the most appropriate anesthetic agent; and (3) a better understanding as to the preoperative care of those patients who constitute definite risks.

Of course, there is rarely a single cause for death. Usually a combination of factors is present, all of which contribute their share to the final outcome. Therefore, these cases have been grouped according to the underlying mechanisms concerned.

These are the "atria mortis" which according to Oertel was the term used by

TABLE I  
TWENTY-THREE OPERATING ROOM FATALITIES  
Predominating Causes of Death

	No. of Cases
I. Cardiac	3
II. Asphyxia	5
III. Shock	7
IV. "Pleural shock"	2
V. Air embolism	2
VI. Anesthesia	4
Total .	23

the ancient physicians to denote the cerebral, respiratory and cardiac types of death. Accessory factors having any bearing on the final outcome are included in Table II.

### CASE REPORTS

In the interest of brevity only representative cases from each group are presented in full. It is immediately apparent that many different mechanisms are often at play in each case. These mechanisms and other factors of importance are presented in the form of a discussion at the end of the presentation of case reports. In the consideration of these cases it should be kept in mind that in the ten-year period from which these cases were taken there has been much improvement in the administration of anesthesia. In the light of present knowledge, anesthetic agents used in certain cases several years ago, would not be used in those same instances now.

*I. Cardiac.* In the cardiac group of three cases there were two cases of aortic stenosis with insufficiency and one case of hypertensive cardiovascular disease with aortic insufficiency. This last patient had a blood pressure of 150/80 and was con-

\* From the Department of Surgery, Royal Victoria Hospital, Montreal.

TABLE II

Case No.	Sex	Age	Operation	Diagnosis	Cause of Death	Contributory Cause	Anesthetic Employed	Anesthetic of Choice
I	M	18	Appendectomy	Chronic appendicitis	Aortic stenosis	.....	Ether	1. Cyclopropane 2. Ether
II	M	54	Herniotomy	Inguinal hernia	Cardiac decompensation	Spinal anesthesia	Pontocaine (spinal)	Local and gas
III	F	22	Craniotomy	Glioma of cerebellum	Aortic Mitral Trikuspid } stenosis	.....	Local and ether	1. Local 2. Ether
IV	M	52	Thoracotomy	Carcinoma of bronchus	Aspiration of pus	.....	Chloroform and N <sub>2</sub> O	1. Cyclopropane 2. N <sub>2</sub> O
V	M	75	Incision and drainage abscess of neck	Abcess of neck	Edema of glottis	Carotid sinus reflex	Local	Local
VI	F	16	Thoracotomy	Malignant thymoma	Compression of trachea	Avertin and gas anesthesia	Avertin and N <sub>2</sub> O	Cyclopropane (intratracheal)
VII	M	42	Thyroidectomy	Lymphosarcoma of thyroid	Compression of trachea	.....	Cyclopropane (intratracheal)	Cyclopropane (intratracheal)
VIII	M	50	Second stage thoracoplasty	Pulmonary tuberculosis	Decreased vital capacity	1. Brown atrophy of heart 2. N <sub>2</sub> O anesthesia	N <sub>2</sub> O	1. Cyclopropane 2. Spinal
IX	F	16	Pneumonectomy	Lung abscess	Pleural shock?	Status thymicolumphaticus?	Local and N <sub>2</sub> O	1. Cyclopropane 2. Spinal 3. Local
X	M	56	Pneumonectomy	Lung abscess	Pleural shock?	Status thymicolumphaticus?	Local	1. Cyclopropane 2. Spinal 3. Local
XI	M	41	Repair of perforated ulcer	Perforated peptic ulcer	Shock	Prolonged reanembency—"sub-lethal shock"	Local	Local
XII	M	52	Repair of perforated ulcer	Perforated peptic ulcer	Shock	Spinal anesthesia	Spinal	1. Spinal 2. Perhaps local
XIII	M	28	Pyclotomy for stone	Abscess left hip; nephrolithiasis	Shock	Prolonged reanembency—"sub-lethal shock"	1. Avertin and gas 2. Ether	Cyclopropane
XIV	M	19	Appendectomy	Appendiceal abscess and pyelophlebitis	Shock	Severe toxemia	Gas and ether	Cyclopropane
XV	F	49	Appendectomy	Perforated appendicitis; peritonitis	Shock	.....	N <sub>2</sub> O and ether	1. Spinal 2. Local and gas
XVI	M	57	Cholecystojejunostomy	Carcinoma of head of pancreas obs. jaundice	Shock	Spinal anesthesia	Spinal	Spinal
XVII	M	37	Gastrostomy	Bleeding peptic ulcer	Shock	.....	Spinal	1. Local 2. Cyclopropane 3. Spinal
XVIII	M	35	Pneumonectomy	Bronchietasis	Air embolism	.....	N <sub>2</sub> O (intratracheal)	Cyclopropane (intratracheal)
XIX	M	23	Lobectomy	Bronchietasis	Air embolism	.....	Chloroform and N <sub>2</sub> O	Cyclopropane (intratracheal)
XX	F	34	Delivery	Pregnancy	Chloroform	.....	Chloroform	1. Cyclopropane 2. Ether
XXI	F	38	Appendectomy	Appendicitis; localized peritonitis	Gas and ether	Unknown factors	N <sub>2</sub> O and ether	1. Spinal 2. Ether
XXII	M	64	Exploratory	Adenocarcinoma of sigmoid	Spinal anesthesia	.....	Spinal	Spinal
XXIII	M	63	Gastrostomy	Myosarcoma of tongue	Spinal anesthesia	Aspiration pneumonia	Spinal	Local

sidered to be decompensated. Each of the first two patients, although compensated, had a blood pressure of 80/60. In all three cases death was rather rapid and unexpected.

**CASE I.** A male, age eighteen, with acute appendicitis, had been known for years to have heart disease. There was cardiac enlargement, aortic systolic and diastolic murmurs and a blood-pressure of 80/60, but there was no evidence of decompensation. Operation was performed under ether anesthesia for a period of forty-five minutes. He breathed poorly throughout. Respirations were 30 to 40 per minute, and pulse was 110 to 120. As the operation came to a close, both respiration and pulse ceased quite suddenly. The usual methods of resuscitation were tried without avail.

At autopsy the heart was quite large, weighing 670 Gm. and there was a well marked aortic stenosis superimposed on a bicuspid aortic valve. The aorta was small, measuring only 3.5 cm. in circumference.

**Comment.** The choice of anesthesia was considered to be a good one, as it was possible to give an excess of oxygen along with the ether. However, cyclopropane would have been a better choice, and perhaps the operation could have been performed even under a local anesthetic.

**CASE II.** A male, age fifty-four, with a right indirect inguinal hernia, had hypertensive cardiovascular disease of at least five years' known duration. There was a history of dyspnea on exertion and ankle edema, and physical examination revealed cardiac enlargement, aortic, systolic and diastolic murmurs, and a blood pressure of 120/80.

Two to three minutes after the injection of spinal anesthesia the blood pressure dropped to zero and the patient expired. At autopsy the premortem diagnosis of hypertensive cardiovascular disease was confirmed.

**Comment.** The fatality in this case may be considered as due to a questionable choice of an anesthetic in a poor risk patient since the greatest drop in blood pressure usually occurs within the first fifteen minutes of spinal anesthesia. In this case local and gas would have been the

anesthesia of choice. Local anesthesia alone was not used as the hernia was a large one, and an attempt at fascial repair was going to be made. In this case the cardiovascular system was already impaired, and oxygenation of the blood was being carried out at a great expense of energy and with only a small margin of safety.

**II. Asphyxia.** **CASE V.** A male, age twenty-five, was admitted to the hospital in *extremis*. There was considerable respiratory distress and he gave the history of having been unable to swallow some hours prior to admission. There was a phlegmon on the right side of his neck. He was given oxygen by mask in the ward, and then later taken to the operating-room where incision and drainage were carried out under local anesthesia. During the operation, respirations gradually became slower and oxygen was then given by intratracheal catheter but the respirations finally ceased. There had been no struggling at any time during the operation.

At autopsy an abscess was found behind the left tonsil. There was arteriosclerosis, some cardiac enlargement and dilatation, early bronchopneumonia of the left lower lobe and a purulent bronchitis.

**Comment.** It was believed that this patient died from asphyxia, the result of massive edema of the glottis. A gradual slowing of the respirations with deepening cyanosis, as present in this case, is characteristic of respiratory failure with terminal exhaustion of the higher centers. However, the fact that death occurred without struggling, although only local anesthesia was used, brings up the question of syncope secondary to a possible carotid sinus effect, which has been mentioned in the literature in similar cases.

In another case, one of an esophageal carcinoma on whom permission for autopsy was refused, death occurred a short time after an incision had been made in the neck. Just before death it had been noted that when the incision was made in the neck, the pulse became slow and strong. The operation was stopped for a moment and the pulse then returned to normal. On

continuing the operation, the patient died. This man was fifty-eight years old and his blood pressure was 158/98. There was no evidence of cardiac decompensation. However, there was a history suggestive of angina pectoris. Examination of the heart had revealed a loud aortic systolic murmur transmitted to the neck vessels.

**CASE VI.** A female, age sixteen, had a malignant thymoma with invasion of the sternum and marked secondary compression of the trachea. The operation was performed under avertin and gas anesthesia. From the start of the operation there was extreme difficulty in breathing; respirations were shallow and the patient cyanotic. After resection of the first rib, it was thought wise not to proceed further as respirations were becoming increasingly weaker. Intratracheal oxygen was tried but the patient expired.

At autopsy the trachea was found flattened and there was moderate pulmonary edema and marked passive congestion of the viscera.

**Comment.** In this case, in view of the respiratory embarrassment, avertin-gas anesthesia was definitely contraindicated. Cyclopropane, which was not available in the year this operation was performed, and oxygen administered by intratracheal catheter would have been the anesthesia of choice.

The marked slowing of the respiratory rate seen in the above case is due to the Hering-Brauer reflex. The marked pulmonary edema so often a feature in these cases is thought by some to be caused by the aspirating effect of a negative alveolar pressure during inspiration. If so, the mechanism of its production differs from that of the pulmonary edema seen in shock, which is probably due to increased permeability of capillary endothelium. However, anoxia in itself causes an increase in the permeability of capillary membranes. Perhaps in both of these instances anoxia is of great importance in the causation of pulmonary edema.

**III. "Pleural Shock."** **CASE IX.** A female, age sixteen, well nourished, was admitted with

a lung abscess. Physical examination was essentially negative except for the abscess in the right lower lobe. The operation was carried out under nitrous oxide anesthesia with the patient in a sitting position. As the pleural adhesions were being cut a vessel was opened by the cautery, which bled for only a few seconds before it was stopped by coagulation around the area. At this moment her heart suddenly stopped beating although respirations carried on for a minute or two.

At autopsy the patient appeared healthy and slightly obese. The mesenteric glands were large. A moderate-sized abscess was found in the right lower lobe.

**Comment.** If the death had been due to gas anesthesia, one would expect respiratory failure to precede failure of the circulation. Was death due to air embolism? No pathological evidence was found to substantiate this belief. Was this a case of status thymicolymphaticus? Just what is the so-called "pleural shock"? An attempt to answer these questions will be made in the discussion which follows.

**CASE X.** This case was similar to the previous one in that cautery pneumonectomy was again being carried out for lung abscess. A male, age fifty-six, was operated upon under local anesthesia which was not altogether satisfactory as the patient experienced some pain during the use of the cautery. Quite suddenly, when about a third of the way through the operation, the patient seemed to go into syncope. He lost consciousness, the respirations became shallow and the skin cyanotic. The respirations then ceased and shortly afterward the heart stopped beating.

Autopsy showed the body to be well developed and slightly obese. The heart weighed 330 Gm. and there was interstitial fibrosis along with some microscopic hypertrophy of the muscle fibers. There were no other findings of note.

**Comment.** This case is interesting in that interstitial fibrosis of the myocardium is frequently found in cases diagnosed as having status thymicolymphaticus, and it is considered by some as one of the characteristic, although not constant, features of the syndrome.

*IV. Shock.* CASE XII. A male, age fifty-two, was admitted to the hospital with a perforated gastric ulcer of some hours' duration. Spinal anesthesia was given as the patient was known to have bilateral pulmonary tuberculosis. An urgent case, he was an extremely poor risk with a preoperative blood pressure of 90/64 and a pulse of 140. The operation lasted thirty-five minutes and the patient died some forty minutes later in the operating room. He had not been moved back to the ward because of his critical condition.

At autopsy the body was well nourished. The positive findings were limited to the lungs and abdomen. The lungs were heavy and voluminous, weighing 520 and 610 Gm. and microscopic study showed edema and dependent congestion. There was a left-sided hydrothorax of 400 cc. The perforated ulcer was found and the surrounding peritoneum was seen to be covered with a fibrinous exudate.

*Comment.* Obviously, this case is one of shock due to the overwhelming reaction caused by perforation of a peptic ulcer. The use of spinal anesthesia in the presence of such low blood pressure and even the trauma of surgery itself had some bearing on the final outcome, but their effect must have been very minor as compared to the shock resulting from intestinal perforation.

CASE XIII. A male, age twenty-eight, had developed osteomyelitis of the left hip and femur as the result of a gunshot wound in the left hip. The bladder had also been perforated at the time of injury and there was a vesical sinus draining through the hip wound. His hospitalization was a long one and as the result of urinary infection together with prolonged recumbency and stasis in the urinary tract, he developed nephrolithiasis. A pyelotomy was performed under avertin and ether anesthesia. His condition which was rather poor at the start became rapidly worse. The pulse was rapid and thready. While the wound was being closed he stopped breathing and expired.

At autopsy he was seen to be poorly nourished. The right side of the heart was moderately dilated. The viscera were congested and the lungs showed bronchopneumonia and congestion at both bases. There was also a pyonephrosis (right) with bilateral septic renal

infarcts. There was exudative purulent osteomyelitis of the left hip and femur.

*Comment.* Death in this instance was due primarily to shock to which a weakened physical state secondary to prolonged hospitalization must have played an important part. It might also be well at this point to mention the importance of psychic factors in regard to operative risks. It is believed that psychic trauma will also bring on a shock state due to the bombardment of the neurovascular apparatus with nervous impulses. In this particular case, the patient, due to sepsis and prolonged hospitalization, had deteriorated considerably from the standpoint of morale. It was noted on frequent occasions that even the giving of a hypodermic resulted in considerable pain and mental anguish. The patient also exhibited fear and extreme nervousness prior to operation. Quite possibly the nervous element in this case played an important rôle in producing his shock state as found at operation.

*V. Air Embolism. Cases XVIII AND XIX.* Both of these cases were lobectomies for bronchiectasis. In one of them the right pulmonary vein was cut, in the other, four or five small branches of the pulmonary vein.

Autopsy findings in both cases were characteristic. There was frothy blood in the heart, air in both the coronary and cerebral arteries, and petechial hemorrhages in the cerebral cortex and subarachnoid space.

*VI. Anesthesia.* Anesthetics *per se* have accounted for only a relatively small number of these deaths. In two of the twenty-three cases spinal anesthesia was held to be the cause of death, in one of them chloroform was held responsible and in the other ether was the predominating factor.

CASE XX. A female, age thirty-four, healthy, para iv, gravida v, prior to delivery had been given 3 gr. of nembutal. She was given a light chloroform anesthesia, not exceeding five minutes. Labor was short and spontaneous and the blood loss small. While the placenta was being delivered, maternal respirations became labored, she became deeply cyanosed, and in a very

short time pulseless. She died twenty minutes postpartum.

At autopsy there were focal degenerative changes in the liver (central necrosis). There were petechial hemorrhages in the liver, gastrointestinal tract, renal pelvis and bladder. The right side of the heart was dilated and there was marked cloudy swelling of the heart and viscera.

CASE XXI. A male, age thirty-eight, was admitted with acute appendicitis and localized peritonitis. On admission his temperature was 102°F., pulse 136, respirations 26, blood-pressure 140/90 and white blood cells 17,500. Appendectomy with drainage was carried out under nitrous oxide and ether anesthesia which lasted for one hour and fifteen minutes. During the removal of the appendix the patient developed marked tremors, first of the upper half of the body and later extending to the whole body. These later progressed to convulsive seizures which apparently became gradually less severe. By the time the operation was finished, the respirations were irregular and there were breath holding spells during which he would get quite cyanotic.

At autopsy the body was considered to be well developed. The trachea was edematous and there was marked pulmonary edema and congestion. The left chest contained 50 cc. of fluid. There was congestion of the bowel and beginning peritonitis in the right lower quadrant.

*Comment.* This patient who was operated upon on a very hot day in August, represents one of the so-called "ether convulsions." As is usually the case, the patient was very sick with evidence of toxemia.

CASE XXII. A male, age sixty-four, lapsed into a semiconscious state a few minutes after having been given spinal pontocaine. He was taken into the operating room where an intravenous injection was started. It was then decided to go on with the operation. However, as soon as the incision was made the respirations ceased. The usual restorative measures were tried, including massage of the heart, which kept the heart beating for only a short while.

At autopsy nothing in particular was found to explain the death, so it must be considered as due to respiratory failure on an anesthetic basis.

CASE XXIII. This is a case of a male, age sixty-three, with a myosarcoma of the tongue of nine years' duration on whom a gastrostomy had been planned. At the time of operation the patient was slightly dyspneic and propped up in bed. He was given pontocaine spinal anesthesia with a resulting anesthetic level up to the fourth dorsal vertebra. Shortly afterward respirations eased and he became unconscious. Adrenalin was given along with artificial respiration. An airway was then inserted. Asphyxia had resulted as the intercostal muscles were thrown out of action in a man whose respiratory physiology was already impaired. He was then kept in good condition during the operation by oxygen and carbon dioxide under positive pressure. When this was discontinued prior to return to the ward, he again underwent respiratory failure, which this time did not respond to treatment.

At autopsy the lungs were found to be voluminous and heavy, weighing 715 and 1,065 Gm. There was moderate pulmonary edema. Abundant fat globules were also found in the bronchi and alveoli, both grossly and microscopically, and this was associated with an exudative and productive pneumonia.

*Comment.* Obviously, this is a case which should have been done under local anesthesia. The tumor of the tongue causing a partially obstructed airway, and the diffuse lung infection, supposedly an aspiration pneumonia, contributed strongly to the final outcome.

#### DISCUSSION

*Anoxia.* In searching for some feature common to these cases of operating room deaths, it became immediately apparent that in all but a few of them asphyxia or oxygen deprivation of the tissues was a factor of the greatest importance. In these cases the progression of oxygen want or anoxia could be followed clinically, and at autopsy the effect of this anoxia could readily be seen.

Because we believe that anoxia may be considered the common denominator of many of our cases, a short résumé of this subject has been undertaken.

By definition, when the tissues fail to receive an adequate supply of oxygen, we

say there is anoxia, or oxygen want. This may come about in one of several different ways, and these Barcroft has separated into three groups: (1) Anoxic anoxia, which is that state resulting from defective oxygenation of the blood; (2) anemic anoxia, in which there is a lack of or inactivation of hemoglobin; (3) stagnant anoxia, which is due to slowing of the circulation through the capillaries and smaller blood vessels. A fourth subdivision was later added, by Peters and Van Slyke, (4) that of histotoxic anoxia, in which the tissue cells are inactivated or drugged so that they cannot utilize the available oxygen.

It is obvious that any of these several mechanisms may lead to asphyxia. However, it is usually a combination of several or even all of these types which results in serious complications. For example, while emphysema will result in a degree of anoxic anoxia due to *decrease in alveolar aeration*, secondary anemia would result in a degree of anemic anoxia, surgical shock in stagnant anoxia, and preoperative medication such as nembutal and morphine in histotoxic anoxia. If all four of these conditions were present at the same time, as is conceivable during the course of an operation, the sum total might easily be more than the patient could stand.

McClure et al.<sup>1</sup> have discussed this subject and the effect of the various anesthetic agents in respect to anoxia. A few of their conclusions are of interest. For example, they point out that 80 to 95 per cent concentration of nitrous oxide in the blood is necessary for good anesthesia. However, this leaves less oxygen than necessary for maintenance of an adequate oxygen tension in the blood. As a result, therefore, anoxic anoxia is produced, first by a reduction of arterial oxygen tension, and then latter by depression of the respiratory center. On the other hand, the action of avertin is different in that it produces anoxic anoxia through respiratory depression and then by circulatory depression a stagnant anoxia. However, the most widespread effect is probably

that of the barbiturates. They are known to act through the di-encephalon, and they have both sedative and hypnotic action. There is an initial circulatory depression, thus a stagnant anoxia, then later respiratory depression with resulting anoxic anoxia. However, the most important effect is on the cellular respiration, histotoxic anoxia. Finally, in spinal anesthesia a degree of circulatory depression may result from paralysis of the vasoconstrictors in anesthetized areas and with this there comes a stagnant anoxia. But it is probable that most of the fatal accidents due to spinal anesthesia are secondary to paralysis of the phrenic mechanism, the intercostals, or of the respiratory center.

It follows, therefore, that those cases which exhibit a relative anoxia prior to operation, no matter what the cause, are operative risks. This is because the anoxia already existent is almost certainly to be made worse by the addition of other types of anoxia through the use of preoperative medication and anesthesia, and through shock due to various reasons such as psychic trauma or surgical trauma secondary to the operation itself.

The discussion of the following seven subjects is of importance as they have bearing on the various causes of death in the different cases presented in the case reports.

1. *Aortic Stenosis.* Aortic stenosis is now well known to be a cause of sudden death. Marvin and Sullivan,<sup>2</sup> in 1935, reviewed this subject and out of 228 cases of aortic stenosis in which autopsies were performed they found seventeen cases of sudden death. The mechanism concerned is a moot point. The available evidence accumulated by them did not support the belief that syncope was due to cerebral anemia dependent upon inability to force blood through the stenotic aortic orifice. They believed that it was due most probably to a hyperactivity of the carotid sinus reflex or some reflex involving the same central and efferent pathways. As for the aortic stenosis found in this case, it was not

definitely proved to be rheumatic in origin nor was there any history of rheumatic fever. Quite possibly, the congenital bicuspid valve played an important part in its etiology.

2. *Carotid Sinus Reflex.* The carotid sinus reflex as a cause of sudden death in surgical cases has been mentioned a number of times in the literature. Cohn,<sup>3</sup> Downs,<sup>4</sup> and Rovenstine and Cullen<sup>5</sup> mention that in their experience "sudden deaths following incision and drainage of abscesses in the neck are not rare." The anesthetic agents, nitrous oxide and chloroform, certain barbiturates, avertin and morphine, all have been found experimentally to sensitize the carotid sinus (Downs<sup>4</sup> and Rovenstine<sup>5</sup>).

According to Soma Weiss,<sup>6</sup> 70 to 78 per cent of those people with hypertensive cardiovascular disease or advanced arteriosclerosis have a hyperactive carotid sinus reflex. This is interesting in view of the two cases presented above, both of whom were well along in years and showed evidences of arteriosclerotic changes. Robinson<sup>7</sup> and Weiss et al.<sup>8</sup> have written thorough discussions of the syndrome of the hyperactive carotid sinus reflex.

3. "*Pleural Shock.*" About "pleural shock" little is known and very little has been written. It is a term used to denote cases of unexplained sudden death occurring during the course of thoracentesis or other surgical procedures in which the pleura is irritated. Two theories have been suggested in explanation of this occasional but yet all too frequent catastrophe (Graham<sup>9</sup>). The first is that of cerebral air embolism, and the second is that which presupposes some unknown pleural reflex, in the nature of a vasovagal reflex. Frequently, when the pleura is irritated experimentally, usually an inflamed pleura, there is an associated marked fall in the blood pressure. This reflex is assumed to be transmitted through the vagus nerve. More credence, however, has been placed in the theory of cerebral air embolism. It has been shown that very small amounts of air injected rapidly into the pulmonary veins

will occasionally cause death, whereas much larger amounts injected into a systemic vein will have no harmful effect.

4. *Status Thymicolumphaticus.* Another interesting subject which is of importance as far as this paper is concerned is that of status thymicolumphaticus. Death in several of the above cases remains unexplained and as they presented several characteristics suggestive of this syndrome, this summary is included.

Although it was the conclusion of a committee investigating status lymphaticus in the British Isles<sup>10</sup> that there was "no evidence that the so-called 'status thymicolumphaticus' has any existence as a pathological entity," nevertheless that there is such a diathesis is commonly held and that such cases are subject to sudden and unexplained death from what would appear to be trivial causes is a common observation. Symmers<sup>11</sup> found 249 cases out of 4,000 autopsies in Bellevue Hospital, New York, or 6.2 per cent of all cases. They came from all races in a proportion of males to females of 6:1. He found that a combination of hereditary constitutional anomalies may be found including: (1) certain peculiarities of bodily configuration; (2) preservation or even hyperplasia of the thymus at an age when involution might be expected; (3) hyperplasia of lymphatic tissue in spleen, intestines and elsewhere; (4) changes in hair distribution; (5) hypoplasia of the vascular system. Michael<sup>12</sup> believes that certain cases of operative death can be explained on this basis.

5. *Shock.* Shock forms by far the largest group of postoperative deaths, and it also accounts for the largest number of operative deaths. It is the main problem which both the anesthetist and surgeon have to contend with. Its causes are many and complex and its management is an urgent one. Its primary effect is that of a stagnant anoxia, and the pathology of shock is basically similar to the pathology of anoxia, due to whatever cause.

Briefly these changes consist of capillary dilatation with occasional small perivascular extravasations of blood. The viscera show passive congestion, and the lungs as a rule show pulmonary edema. Sometimes a diffuse hemorrhagic infiltration is present throughout the lung parenchyma. Pulmonary edema evidently is dependent upon the duration of the shock state, as patients dying early in shock do not show it. The diagnostic feature, clinically speaking, is that of hemoconcentration. This state is found in all cases except where the shock state is secondary to hemorrhage and then one finds hemodilution.

An important concept is, as Moon<sup>13</sup> points out, the liability of a vicious circle. This applies to those cases in which the systolic blood pressure has been hovering around 70 to 80 for a matter of hours. The danger in these cases is that tissue anoxia once having set in will lead to acidosis and defective metabolism, with resultant capillary atony and then a consequent reduction in blood flow and thus greater anoxia.

Nowadays we are all aware of shock, but that there is a condition which we might call a state of chronic shock or what Moon calls sub-lethal shock<sup>14</sup> we are inclined to ignore. Here due to malnutrition, wasting illnesses, and prolonged recumbency, a pathological state develops which is akin to shock, and as Moon shows predisposes a terminal bronchopneumonia. These cases then would naturally be poor operative risks, and any medication or anesthetic known to aggravate shock would be contraindicated. Such a condition we have in Case XIII.

6. *Air Embolism.* Experimental work by Joannides and Tsoulos<sup>15</sup> is interesting in this regard. They found that the speed of air embolism is as important as the amount of air. They injected 200 cc. of air into the femoral vein of dogs and found that it was a fatal amount when given in less than five minutes. However, if this same amount of air was given in thirty minutes or over it was not fatal. This would be an argument in favor of slow dissection

especially when operating in a region where veins are known to have a negative pressure, such as the chest and neck. However, the important fact in the consideration of these two cases is, as mentioned above, that only relatively small amounts of air need be injected into the pulmonary veins in order to cause death. This is because air sucked into the pulmonary circuit is immediately pushed into the cerebral arteries along with the rest of the systemic circulation.

The mechanism of death in these cases is due either to (1) asphyxia and anoxemia, as the heart and arteries are filled with froth, and energy is expended in mere churning, or (2) central anemia because of obstruction in the cerebral vessels due to air bubbles. Anoxemia results, followed by a constrictor paralysis which is in turn followed by dilatation of the vessels and subsequent diapedesis of red blood cells. This explains the petechial hemorrhages so commonly present in these cases.

7. *Anesthesia.* In general we might say that anesthesia has had to take the blame for a greater number of operating room fatalities than in our opinion has been warranted. It is far too easy to dismiss a case as an anesthetic death without due consideration of the many physiological factors entering into the picture. However, it is true that anesthetic deaths are all too common and could perhaps be diminished in number by proper preoperative care, wise choice of the anesthetic agent, and consideration of the various secondary factors which might make the patient a definite risk.

Gwathmey<sup>16</sup> found by reviewing the records in the Chief Medical Examiner's Office in New York City that from 1928 to 1932 there were 219 deaths, or forty-four per year. These were considered to be true anesthetic deaths, to which no pathological condition of the patient could be found to have contributed. He stressed the importance of proper preliminary medication in the prevention of anesthetic deaths with the consideration of psychic as well as organic factors. In this paper we do not

intend to go into the physiology of anesthesia. However, it is perhaps expedient to mention a few pitfalls that have been brought to our attention by a study of our own cases:

*Local Anesthesia.* This we will dismiss with little more than mentioning an important experimental observation by Beecher<sup>17</sup> that while 40 mg. per kg. of novocaine when injected rapidly intravenously will kill a cat, when injected slowly 400 mg. per kg. may have no harmful effect at all. That there are cases on record of sensitivity to novocaine is well known. This has been one of the suggested reasons for the so-called "pleural shock." However, we do not believe that this had any bearing on our own series of cases.

*General Anesthesia.* As for general inhalation anesthesia, there is a long list of available agents, and they have many different indications and contraindications. Some agents, such as chloroform, have been largely condemned except under certain rare circumstances. Beecher<sup>17</sup> states that there is absolutely no margin of safety in chloroform anesthesia; 20 to 40 mg. per cent will seriously impair heart action, and yet 18 to 40 mg. per cent is necessary for full narcosis. The mechanism of death is considered to be cardiac. The drug is known to be toxic on the heart long before it is on the respiratory mechanism.

*Ether Anesthesia.* Ether convulsions are phenomena about which nothing positive is known. Many theories have been advanced concerning their etiology. Dodd<sup>18</sup> believes that atropine is partly responsible; Rosenow and Tovell<sup>19</sup> thought it might be a neurotoxin liberated from streptococci. Low serum calcium has been held responsible in some instances. Quite likely, however, many more factors are responsible. These cases almost invariably occur in the heat of the summer and they usually show evidence of toxemia.

*Spinal Anesthesia.* As stated before, fatal accidents due to spinal anesthesia probably occur secondarily to paralysis of

the phrenic mechanism, the intercostals or of the respiratory center.

#### SUMMARY

1. Twenty-three consecutive cases of sudden operative deaths in which autopsies were performed occurring during a ten-year period in the Royal Victoria Hospital have been reviewed from both the clinical and the pathological points of view.

2. The purpose of this survey was to throw some light on the mechanisms concerned in such deaths, thereby enabling us to give more care to the preoperative and operative management of the different cases.

3. We believe that by applying Barcroft's classification of the different types of anoxia to the majority of these cases, it enables us to understand more readily the various mechanisms involved.

4. Other factors of importance in the causation of operating room fatalities as determined from our cases include aortic stenosis, cardiac decompensation, asphyxia, shock, so-called "pleural shock," hemorrhage, status lymphaticus, air embolism and anesthetic agents.

5. Finally, because of the various causes of death, the various precipitating factors involved, and the many different physiological mechanisms at work in these cases, it is apparent that to obtain the greatest degree of safety each poor risk patient must be treated individually by both surgeon and anesthetist and through consultation a definite plan of action decided upon.

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# DIAGNOSIS AND TREATMENT OF ACRAL GANGRENE\*

PAUL D. ABRAMSON, M.D.

On Surgical Staff, North Louisiana Sanitarium  
SHREVEPORT, LOUISIANA

AT first thought, one might suppose that the diagnosis and treatment of gangrene of the extremities is not a very involved subject. The diagnosis of gangrene is usually self-evident, and the treatment must, ultimately, be amputation in some degree or other. But a little thought will reveal that the subject is far from being a simple one. Gangrene is the dramatic terminal picture of deficient circulation but is not, in itself, an acceptable diagnosis. Instances of acral gangrene differ as to etiology and pathology and there is a concomitant difference in the treatment and prognosis. Two cases, for example, may appear quite similar on superficial examination and yet one may successfully be treated by an auto-amputation, or at worst a very minor local amputation while the other may require a radical high amputation for its correct management. Not only will a proper and complete diagnostic study in cases of gangrene of the extremities permit of intelligent and correct therapy, but more important, a full knowledge of the causes and types of gangrene is more likely to make the clinician "gangrene conscious" so that whenever possible he can forestall its development by the earlier diagnosis of certain predisposing vascular disorders.

## CLASSIFICATION

Acral gangrene may be divided into two large clinical groups: The first group includes cases of gangrene developing in a limb without previous significant arterial disease, the first inkling of a pathological condition being the development of impending gangrene. The second group includes those cases in which there has been pre-existent arterial disease and in which it

should have been possible to foresee the eventuality of gangrene. The responsibility of the physician, prophylactically speaking, is considerably greater in this latter group

## GANGRENE DEVELOPING IN A LIMB WITHOUT PREVIOUS SIGNIFICANT PERIPHERAL VASCULAR DISEASE

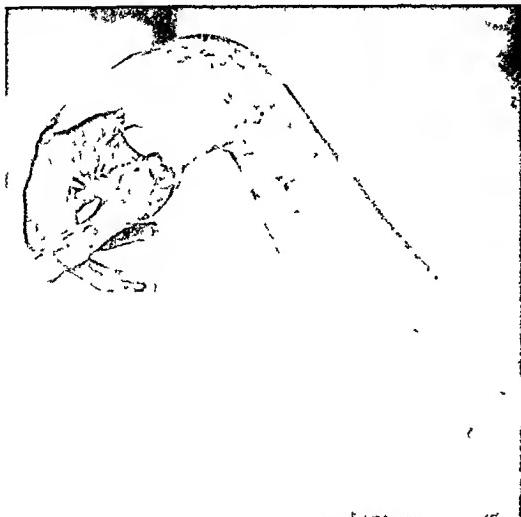
Here we find those cases in which gangrene develops or threatens because of (a) trauma to a main arterial trunk, (b) thermal factors, (c) embolism, (d) chemicals or drugs, (e) thrombosis associated with postural stasis or systemic disease and (f) local infections.

It is not surprising that in this group, without pre-existing significant vascular disease, gangrene is never given a thought until there dramatically develops a cold, pulseless extremity associated with such other characteristic signs as a mottled appearance, anesthesia or paresthesia, loss of function and perhaps pain. Yet even in this group of cases a certain number could be prevented by the avoidance or protection against certain factors which are known to predispose to the development of such gangrene.

(a) *Trauma to a Main Arterial Trunk.* This is, perhaps, the least preventable of all forms of gangrene. There are various types of injuries to main vessels, any of which may produce varying degrees of gangrene distal to the injury. Such injuries vary from severance of the trunk necessitating ligation, to internal hemorrhage producing an aneurysm (false) which, by pressure, obliterates the main trunk. Whether or not gangrene develops after such an injury obviously depends upon whether or not sufficient collateralization can develop.

\* From the Peripheral Vascular Clinic, Charity Hospital, and the Surgical Section, North Louisiana Clinic.

This, in turn, depends upon two factors: (1) the overcoming of vasospasm in collateral vessels (vasospasm being invariably



**FIG. 1.** *Vasospastic gangrene:* Following an injury to the right subclavian artery, the right upper extremity became pulseless and cold, gangrene and ischemic contractures resulting as pictured. The artery was not severed, simply injured, because within a comparatively short time excellent and apparently normal circulation returned to the extremity. The gangrene and other damage evidently was the result of intense traumatic vasospasm. This could probably have been prevented by immediate regional sympathetic block. Such a chemical section should be empirically done in all cases of trauma to the big vessels, to counteract the invariably associated vasospasm.

associated with such trauma) and (2) the collateral-forming potentialities of the region concerned.

Thus it has been shown<sup>80,86,107,120</sup> that if an artery is wounded there invariably develops a varying amount of vasospasm in the other vessels of the extremity; and Heidrich (quoted by deTakats<sup>35</sup>) showed that the percentage of gangrene after arterial ligation varied from 100 per cent after aortic or common iliac ligation to 0 per cent after ligation of the radial, ulnar or posterior tibial arteries, with a 37.2 per cent likelihood of gangrene following ligation of the popliteal as compared to 21.8 per cent following ligation of the common femoral. The "collateral-forming" potentialities ("blutegefühl") depend not only on the vessel or region involved but also

upon the condition of the vessels. Trauma to a vessel in an extremity in which there is already a vascular pathological condition is



**FIG. 2.** *Gangrene from frost-bite:* The essential pathological status of such gangrene is an initial vasospasm with secondary thrombosis. Such gangrene is entirely preventable by proper protection from undue exposure. The initial treatment is counteraction of the underlying vasospasm. Débridement of the localized gangrene can be safely done, as it can be done in most cases of gangrene which develops in a limb without previous vascular disorders.

obviously more serious than if the vessels be normal.

The fact that gangrene can result primarily from venous disorders rather than arterial disorders is frequently overlooked. It has been pointed out that venous thrombosis due to trauma or phlebitis can produce a reflex vasospasm of the arteries<sup>14,34,35,85,113</sup> which may, at times, cause sufficient arterial obstruction to threaten or actually produce gangrene. Moreover, varicose ulcers, the result of simple varicosities or varicosities associated with arteriovenous fistulas, are really localized areas of superficial gangrene from marked venostasis.<sup>5</sup> A too tightly applied cast may cause vascular disturbances principally through its interference with venous circulation.

The treatment of gangrene that results from the traumatic stoppage of blood through the main arterial trunk is aimed primarily at its prevention while it is still impending and before it becomes inevitable. Such treatment seeks the maintenance of effective nutrition until collateralization fully develops. This is accomplished by (1) overcoming vasospasm and (2) vein ligation. Leriche<sup>86</sup> has emphasized the rôle of vasospasm in trauma to, or ligation of,

arterial trunks and has pointed out that if it is necessary to ligate an artery, a segment should be removed between ligatures, this

number of clinicians in treating gangrene which is the result of vascular disorders<sup>12,37,87</sup> as well as of trauma.<sup>1</sup> It has



FIG. 3. Gangrene from embolism: Such gangrene can be minimal as here illustrated, or quite extensive. In the extensive forms vasospasm should be actively combated. Successful embolectomies have been done, but there is some reason to believe that such a procedure can be equalled in results by release of vasospasm. It is sometimes difficult to differentiate thrombosis and embolism, but the treatment in both types of gangrene is essentially the same. The resulting gangrene can be treated by a localized amputation or débridement and good healing of the stump can be anticipated.

seeming to lessen the degree of vasospasm. Other methods he has recommended for combating vasospasm include peri-arterial sympathectomy above the lesion, anesthetic infiltration of the adventitia and chemical or surgical section of the sympathetic flow. Gage and Ochsner<sup>59</sup> have employed sympathetic block in ten cases preliminary to ligation of a main arterial channel and in none did gangrene ensue. Papaverine hydrochloride is likewise useful in overcoming vasospasm.<sup>36,118</sup>

Oppel<sup>116</sup> first suggested the ligation of a vein, the popliteal, in preventing gangrene in which the arterial circulation was deficient, the theory being that this produced a more effective tissue pressure of the available nutritive material by preventing its too rapid removal via the intact venous system. Holman and Edwards<sup>69</sup> showed experimentally that if the vein is ligated higher than the artery, both the blood pressure and the blood flow is increased in the distal stump of the ligated artery. This procedure has been used by a



FIG. 4. Bilateral "juvenile" gangrene: So-called "juvenile" gangrene is not a clinical entity but results from a variety of causes. In this case, the cause was bilateral thrombosis occurring in the course of a systemic infection (typhoid). Amputation was confined to the area of demarcation with good healing of the stumps.

been recommended that whenever it is necessary to ligate a main artery, its satellite vein should likewise be ligated, thus lessening the likelihood of gangrene developing. The value of this procedure, in selected cases, has been shown by the clinical and experimental observations of Brooks and his associates.<sup>22,23,24</sup> However, Leriche<sup>83</sup> has recently pointed out that he believed the value derived from vein ligation is the result of relaxation of vasospasm and he has abandoned the procedure for more direct methods of relaxing vasospasm.

We have seen no results whatsoever in the use of suction-pressure treatment in the development of collaterals in cases of traumatic interruption of a main arterial channel; perhaps this is because the benefits

from this form of treatment are evidenced too slowly to be of practical value.

In summary, then, the treatment of gangrene or impending gangrene following injury to a main arterial trunk is principally the relaxation of vasospasm by novocain block of the regional sympathetics and the use of papaverine. If a main arterial trunk is ligated, its satellite vein is likewise best ligated. Once actual gangrene develops, it can be allowed to proceed to auto-amputation or when well demarcated, a local removal of the dead tissue may be done.

Two additional procedures frequently used are the conservation of the heat of the extremity by wrapping it in sheet cotton or some similar material, and the maintenance of the extremity at a level slightly below that of the heart. The use of the uncontrolled heat (light) cradle and the elevation of the extremity, procedures which are frequently used, cannot be condemned too strongly. This applies to gangrene of any origin (with the possible exception of infectious gangrene, v.i.). As Freeman<sup>57</sup> has pointed out, gangrene results from a discrepancy between the demands of the tissues and the supply of blood to meet these demands. Furthermore, the metabolism of tissue increases directly with its temperature. If a heat cradle is used, it should be carefully regulated to body temperatures.<sup>133,143</sup> If the heat be excessive, the development of gangrene is more likely to be facilitated than prevented. It is usually sufficient to insulate the extremity against loss of heat. As Leriche<sup>86</sup> has pointed out, external heat is of little value as it is not the skin but the deeper structures that need blood and this can be little influenced by external heat. Elevating the leg serves to hasten venous drainage from the part and this is more likely to result in gangrene than if semistagnation is encouraged by keeping the extremity a little below the level of the heart.

(b) *Thermal Gangrene.* As pointed out above, heat, under certain circumstances, may encourage the development of gan-

grene. But it is cold that most typically produces such a lesion, the so-called "frost-bite." Even in the deep South this lesion is occasionally observed.

Theis<sup>147</sup> has pointed out that the pathophysiology of frost-bite is primarily cutaneous vasoconstriction resulting in a short-circuiting of arterial blood directly into the veins. Thus the superficial structures are not irrigated with blood. He divided the lesions into three stages: (1) acute vasomotor ischemia in which the injudicious use of heat may be distinctly harmful because of increasing demands on tissues incapable of meeting them due to the vasoconstriction. If thrombosis does not occur, complete recovery may ensue. (2) Chronic frost-bite or chilblains may follow the acute stage. (3) Necrosis and gangrene may occur if the vasoconstriction is unrelieved and thrombosis occurs.

Brahdy<sup>19a,20</sup> has made some interesting observations on frost-bite among New York City employees. He found that a temperature below 14° F. constitutes an industrial hazard, particularly if the individual has diabetes or arteriosclerosis. The important prognostic point, he found, was the length of exposure after the first symptom. Brahdy has emphasized that the only satisfactory preventative against frost-bite, if cold exposure must occur, is in the use of adequate clothing. We have seen no real benefits from suction-pressure treatment in the few cases that have come under our observation, nor has Brahdy. Murphy,<sup>108</sup> however, has reported good results. If gangrene threatens, the best treatment is the protection of the part against further heat loss and the combating of vasospasm by papaverine or regional sympathetic anesthesia. Once definite gangrene is present it may be allowed to proceed to auto-amputation or a strictly local amputation may be done.

(c) *Peripheral Embolism.* Arterial embolus is of particular interest because it is one of the few acute vascular lesions amenable to radical and at times dramatic surgical intervention. Especially is this true

since the availability of heparin. Yet, because of the intense vasospasm present, sometimes equally dramatic results may be



FIG. 5. Gangrene from thrombosis of the left radial and ulnar arteries: Despite suction-pressure treatment the gangrene progressed until amputation had to be done above the wrist. The etiology was a thrombus, as proved at operation, apparently resulting from stasis from sleeping on this arm, an unusual development. The extension of the gangrene could possibly have been prevented by regional sympathetic block or by heparinization.

obtained from conservative measures directed at relaxing this vasospasm. The principal difficulty, if one contemplates surgery, is the differentiation of embolism and thrombosis.

Embolism usually occurs suddenly with no previous significant peripheral vascular lesion. Usually the process is initiated with sudden severe pain, although this is not invariably present.<sup>95</sup> The clinical findings will obviously vary, depending on the number and location of the emboli; simple superficial areas of gangrene may be present or there may be massive gangrene of an extremity. This is preceded by a pale, pulseless extremity with anesthesia or paresthesia. According to the findings of McKechnie and Allen,<sup>95</sup> 50 per cent of embolic cases progress to actual gangrene.

In 70 per cent of cases the embolus originates in a heart lesion,<sup>76</sup> while it occurs postoperatively in about 14 per cent.<sup>39</sup>



FIG. 6. Infectious gangrene: Particularly in diabetes is it important to determine if the gangrene is primarily due to vascular occlusion with secondary infection or if it is due primarily to a local infection with secondary thrombosis. In cases in which the underlying etiology of the gangrene is infection and thrombosis, local conservative treatment of the infection is in order, with a local amputation of the demarcated area.

According to Pearse, quoted by de Takats,<sup>45</sup> peripheral embolism is more frequent in the common femoral (39.1 per cent) less frequent in the common iliac (14.92 per cent) and brachial (11.93 per cent) and least common in the ulnar (0.33 per cent). Koucky and his associates,<sup>76</sup> at Cook County Hospital, found that the lower extremity was involved in twenty of twenty-five cases. They consider the treatment of peripheral embolism under four types: (1) nonoperative, (2) arteriotomy operations, (3) arteriectomies operations and (4) amputative operations.

It is in the treatment of embolism that papaverine has found its greatest usefulness. Pal,<sup>118</sup> in 1914, first recommended the

use of papaverine to relax smooth muscle. Denk,<sup>36</sup> in 1934, introduced its use to combat vasospasm associated with acute embolism, reporting its use in ten cases. Approximately 50 per cent of cases with embolism failed to develop any gangrene. DeTakats has reported even better results.<sup>43</sup> Papaverine hydrochloride is best administered intravenously in  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. doses, every four to six hours. According to Burnett,<sup>28</sup> embolectomy should be done if definite circulatory improvement has not been noted in two hours. Embolectomy is probably useless after twelve hours, although recovery has been reported after forty-eight hours.<sup>74</sup> Gage and Ochsner<sup>59</sup> have reported four cases of femoral embolism in which the patients were successfully treated by novocain block.

Successful embolectomies have been reported by Linton,<sup>91</sup> Lund,<sup>92</sup> Pearse,<sup>119</sup> Key<sup>74</sup> and others. The use of heparin to increase the clotting time has been of definite value in preventing the occurrence of thrombosis at the site of embolectomy. Leriche<sup>84</sup> has recommended arterectomy, as removing a segment of artery decreases vasospasm in other vessels of the extremity. But vasospasm can usually be overcome by papaverine or novocain block of the sympathetics.

One difficulty in contemplating an embolectomy is in localizing the site of the embolus, for the superficial signs are usually some distance removed from the obstruction. This can be accomplished by palpation of the pulses or better still by oscillometry or arteriography.<sup>151</sup>

If gangrene actually develops, it may be allowed to demarcate well before amputation unless the embolus be infected, in which instance the gangrenous area may become infected. In this case, amputation above the level of infection is frequently indicated, if localization does not rapidly occur.

In summary, the treatment of peripheral arterial embolism is first to combat the associated vasospasm which produces many of the clinical signs. This is best done by papaverine and/or novocain block of the

regional sympathetics. If no improvement is noted in a few hours, and if the site of the embolus can be localized, embolectomy with heparinization (local or general) should be done. If gangrene develops despite these measures, a strictly local amputation can be done unless spreading infection develops.

(d) *Drugs and Chemicals.* Several different drugs and chemicals have, from time to time, been reported as producing gangrene. These include such drugs as carbolic acid, aluminum acetate, lead, carbon monoxide and copper sulfate. But the one of most importance clinically is ergot because of its widespread use.

A number of cases of gangrene have been reported after the use of certain ergot preparations, particularly ergotamine tartrate.<sup>64, 123, 159</sup> Yater and Cahill<sup>159</sup> point out that the ergot may produce occlusion of medium-sized and small arteries and arterioles due to severe vasoconstriction and resulting in thrombosis. Hyaline degeneration of the vessels follows the intense vasoconstriction.

McGrath<sup>93</sup> experimentally produced gangrene in albino rats with ergot and compared the pathological lesion with that found in thrombo-angiitis obliterans.

Ergot should be used cautiously and while it is being used the possibility of vascular lesions should be borne in mind, and its use stopped at the first sign or symptom suggestive of vasospasm. Actively, the vasospasm may be combated with papaverine or novocain block of the regional sympathetics. If gangrene actually develops, it can be treated by local débridement of the devitalized area.

(e) *Thrombosis.* Thrombosis is usually the determining factor in the production of gangrene from any cause. But apparently a thrombus can develop in an artery free from a previous pathological condition due to simple stasis, particularly in old people, and in the course of various infectious diseases in which apparently a local acute arteritis may precipitate the thrombus. Gangrene due to thrombosis has been reported in a variety of infectious diseases

such as scarlet fever, pneumonia, diphtheria, measles and chickenpox.<sup>21,30,103</sup>

Included in this group of cases of gan-

have emphasized, if the primary disorder is one of infection, with adequate deep circulation, the therapeutic indications

*SKETCH ILLUSTRATING HOW GANGRENE MAY RESULT FROM  
DIMINISHED FLOW OR INCREASED TISSUE DEMANDS.*

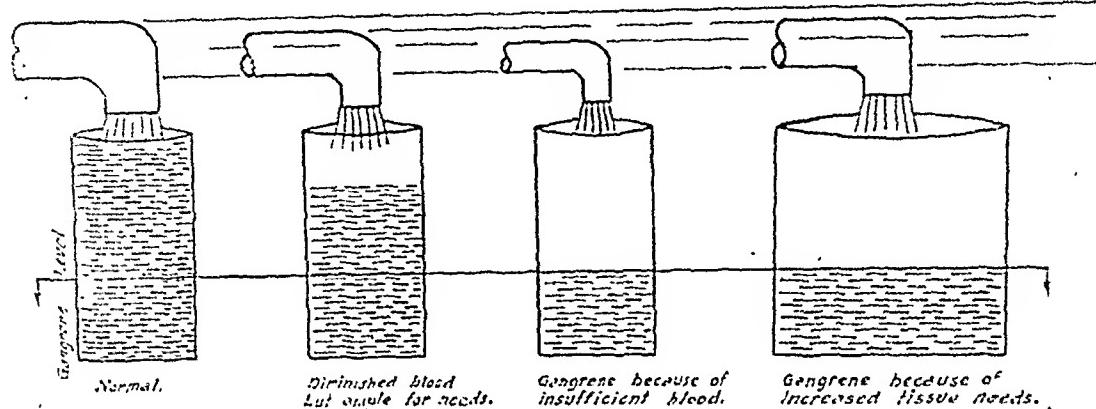


FIG. 7. This sketch illustrates how gangrene may be precipitated by a diminution of the blood flow or by a marked increase in tissue demands in a limb with already diminished blood supply. Such increased demands usually result from injury, excessive heat or cold, or infections.

grene due to thrombosis might be that group of so-called "juvenile" gangrene, although Martin and Shore<sup>104</sup> have reported four cases and reviewed the literature, pointing out that gangrene in children, even when symmetrical, is not a clinical entity. Some may be due to embolism, some to endarteritis and some to autochthonous thrombi. Nearly all reported cases have occurred in the terminal stages or subsequent to generalized infections. Gangrene has even been reported in the newborn.<sup>50</sup>

The treatment in cases of thrombosis is, in the main, like the treatment of embolism, a condition which should be differentiated mainly because of the possibility of doing an embolectomy in the latter cases (v.s.).

(f) *Local Infections.* Sometimes, in the course of an infectious process in a toe, thrombosis occurs in the regional vessels and produces gangrene. Superficially, the gangrene may be indistinguishable from gangrene due to primary vascular disturbances. It is an important differentiation to make. As Williams and O'Kane<sup>153</sup>

are treatment of the infection and a strictly local amputation; if the infection is superimposed upon a primary vascular gangrene, considerably more radical procedures are indicated (v.i.). The differentiation is made by demonstrating the presence or absence of adequate circulation, principally by palpation of the pulses, oscillometry or arteriography. So-called "gas" gangrene is produced by mechanical blockage of the vessels by the large anthrax bacilli; the treatment is primarily toward the treatment of the septicemia, and any amputation done is to eradicate the source of infection.

This question of gangrene developing in an extremity free of previous significant vascular disorders may be briefly recapitulated as follows: In some instances, particularly in instances of trauma and in certain types of thrombosis and embolism, there is no way of preventing the vascular lesion, but the cautious use of ergot, the protection against excessive cold, the prevention of stasis in bedridden patients (if practical) are all prophylactic measures. If

gangrene impends, the prognosis is better than in limbs which are the seat of primary vascular disturbances because it is vasospasm, a remediable condition, that is productive of many of the symptoms. The principal therapeutic measures are (1) relief of vasospasm, (2) the use of the proper level of the extremity, (3) the conservation of the heat of the part, and (4) in embolism the carrying out of an embolectomy. If despite these measures gangrene develops, it usually can be allowed to proceed to well defined demarcation when a strictly local amputation will result in good healing.

#### GANGRENE DEVELOPING IN A LIMB WITH PREVIOUS SIGNIFICANT VASCULAR PATHOLOGY

The vascular lesions that may terminate in gangrene may be conveniently grouped into: (1) *infectious*, including principally (a) thrombo-angiitis, (b) thrombo-arteritis and (c) luetic arteritis; (2) *degenerative*, particularly arteriosclerosis, either senile or diabetic and (3) *neurogenic*, principally Raynaud's disease. With the exception of Raynaud's disease, the vast majority of significant lesions occur in the lower rather than the upper extremities.

In a consideration of this group of cases, it must be realized that the responsibility of the physician is quite great, for in the majority of instances if the vascular pathology be recognized and appropriate measures instituted, gangrene in most instances can be circumvented.

It is not our province here to discuss the diagnosis of peripheral vascular diseases. We would re-emphasize, however, that in the vast majority of individuals a correct diagnosis can be made by utilization of simple clinical methods and without the necessity of resorting to any special diagnostic procedures.<sup>3,4</sup> Clinical evidences of impaired circulation are: (1) intermittent claudication, (2) coldness of the extremity, (3) color changes (cyanosis, ischemia or rubor), (4) absent or deficient circulation as determined by palpation of

the pulses and oscillometry, (5) trophic disturbances or (6) rest pain.

If one would simply routinely palpate the dorsalis pedis and posterior tibial, many cases of vascular disease would not be incorrectly treated for arthritis, fallen arches, neuritis or countless other foot ailments.<sup>31</sup> One should remember the observations of Reich,<sup>125</sup> however, regarding the pulses of the foot, otherwise palpation alone may be misleading. In 500 normal individuals observed clinically, the dorsalis pedis could not be palpated in 4 per cent, the posterior tibial was absent in 5 per cent. In another 8 per cent the dorsalis pedis was found misplaced. These findings were corroborated by anatomical studies.

*The Prevention of Gangrene.* As previously stated, it is not our purpose to discuss the differential diagnosis of the various types of peripheral vascular diseases, but rather the prevention and treatment of gangrene, which may result from such disease. Raynaud's disease has been considered in this group with previous vascular disease. It is realized that there is probably no primary pathological condition in the vascular tree but rather is there an overactive sympathetic system. But this disease gives symptoms months or years before gangrene develops so that if properly diagnosed gangrene can be prevented. If there is no response to conservative protective measures, sympathectomy may be resorted to with good results in many cases. Sclerodactylia is perhaps a more advanced form of Raynaud's disease in which extensive thrombosis and gangrene can occur. Sympathectomy, parathyroidectomy and other procedures have been of questionable value in checking its progress. Those cases with degenerative and infectious vascular disease may be considered as a group when we discuss the question of gangrene prevention.

Assuming that an organic vascular disturbance is known to be present, it is essential that the patient be made "foot conscious." The importance of the pro-

tection and care of the feet cannot be emphasized too often or impressed upon the patient too strongly. While this is

far different." The individual may actually have no symptoms, "their feet may be pulseless but still in a stage of compensa-



FIG. 8. *Thrombo-angiitis obliterans*: A, this shows beginning gangrene in a case of Buerger's disease. B, showing the healing that occurred after fifty-one hours of suction-pressure treatment. As a general rule, treatment is relatively conservative in thrombo-angiitis obliterans and one need not resort to amputation until ample conservative treatment has been found ineffective.

especially so in the case of the diabetic patient, it applies to any patient with an organic obstructive vascular lesion. It is because of the insidiousness of the beginning of gangrene that it is so important to emphasize, to the patient, the potential dangers ahead. As John<sup>71</sup> has said, "If the beginning of gangrene were as noisily ushered in as an attack of biliary or renal colic, the results of treatment would be

tion"<sup>30</sup> and then a precipitating factor causes additional strain on the available circulation, compensation breaks and gangrene threatens.

"The means for estimating peripheral vascular deficiency are almost as accurate as are the means of estimating the efficiency of the blood vessels of the heart and kidney. They are waiting to be put in general use by our profession. Once it

becomes the practice to study the peripheral vessels and advise people when there is a thin margin of safety in the blood supply of their legs, there are many things that can be done to avoid those critical periods of pain, infection, gangrene and amputation. Then, too, there will be a noticeable diminution in the number of patients treated for cramps, metatarsalgia, fallen arches and rheumatism." (Reid.<sup>126</sup>)

The prevention of gangrene in an individual with peripheral vascular disease largely resolves itself into these two things: (1) the intelligent avoidance of precipitating factors and (2) the development of collaterals.

*Avoidance of Precipitating Factors.* There are three things which are particularly likely to cause a break in compensation by placing excessive demands on the available circulation and these are: (1) trauma, (2) infections and (3) thermal changes.

*Trauma and Infections.* These can best be considered together because they are so frequently associated clinically. Trauma may, in itself, by calling forth reparative processes endanger the effective vascularity of a limb, but its principal danger is in producing a lesion which is likely to become infected. In considering the question of trauma, one must think of minimal types which, in themselves, might be considered of little importance and yet in an extremity with deficient circulation may be all that is necessary to turn the tide adversely. The need of a properly fitting shoe, for example, cannot be overemphasized. A shoe too loose may rub sufficiently to produce blisters which are likely to become infected. A shoe too tight will further embarrass the deficient circulation. Patients must be cautioned against trimming corns and ingrowing toe nails as their feet, primarily because of deficient circulation, are more likely to become infected, and once infection develops, the added defensive demands may well strain the effective circulation to a point that "compensation" may break.

Veal and McFetridge<sup>150</sup> analyzed the

precipitating causes of gangrene in 139 of 171 cases. Of these 139 cases, trauma was the precipitating factor in seventy-three cases. In the cases of Buerger's disease, the gangrene resulted from trauma in 28.5 per cent; in the case of arteriosclerotic gangrene, trauma was the cause in 47.2 per cent; in diabetic patients, the gangrene was precipitated by trauma in 68.2 per cent of instances. This indicates that particularly in diabetes is trauma likely to be dangerous; this is undoubtedly because of the increased susceptibility of diabetic patients to infections. Oard et al.<sup>111</sup> found in a series of forty patients with peripheral vascular disease that more than 50 per cent suffered injuries from ill advised treatment. Trauma, they point out, is the most frequent cause of open lesions in a limb with poor blood supply. Similarly, Barker<sup>17</sup> found that in 171 cases of gangrene associated with thrombo-angiitis obliterans, the gangrene followed therapeutic procedures in 35 per cent. In 115 cases of arteriosclerosis obliterans, gangrene followed therapeutic procedures in 39 per cent. Too often has the careless physician observed a red, painful toe and thoughtlessly incised it, thinking it to be an infection, only to realize that severe vascular disease was the cause of the red toe and that injudicious trauma might be the precipitating factor for the development of gangrene.

It is well appreciated that in diabetic arteriosclerosis one of the prime reasons for keeping the patient well stabilized with insulin and diet<sup>1</sup> is to lessen the likelihood of infection developing, because it is likely to precipitate gangrene if it develops in an extremity already the seat of circulatory embarrassment.

*Thermal Changes.* We have already pointed out that excessive heat as well as excessive cold, although operating by different mechanisms, may precipitate gangrene. Heat increases tissue demands, which if the vessels are not able to supply, may cause gangrene. Cold, by causing vasospasm, further embarrasses the circulation and may precipitate gangrene.

*Development of Collateral Circulation.* A consideration of the development of collateral circulation largely concerns itself

repeatedly shown<sup>16,77,101,136,158,109,110</sup> that tobacco smoking has a definite vasoconstrictive action. Although some investigators



FIG. 9. *Thrombo-angiitis obliterans:* Although much cannot be said for the usefulness of the right stump, this picture illustrates the fact that healing in thrombo-angiitis obliterans can frequently be obtained after repeated localized amputations. As a rule, more conservative amputations can be done in thrombo-angiitis than in arteriosclerosis.

with a consideration of the conservative treatment of occlusive peripheral vascular disease, for the aim of such treatment is increased vascularity in the involved extremity. Wright<sup>156</sup> has recently given an excellent summary of this conservative treatment. These therapeutic measures aimed at increasing collateralization may be enumerated as follows:

1. *Active Vascular Exercises.* Buerger,<sup>27</sup> a number of years ago, described the exercises which bear his name. In these exercises the lower limbs are successively raised, lowered and placed level, in an effort to increase vascularity mechanically. Allen<sup>7</sup> has slightly modified these exercises. It is difficult to evaluate the exact degree of improvement such exercises engender, but they have, clinically at least, appeared to be of value and are in widespread use.<sup>72</sup>

2. *Abstinence from Tobacco.* It has been

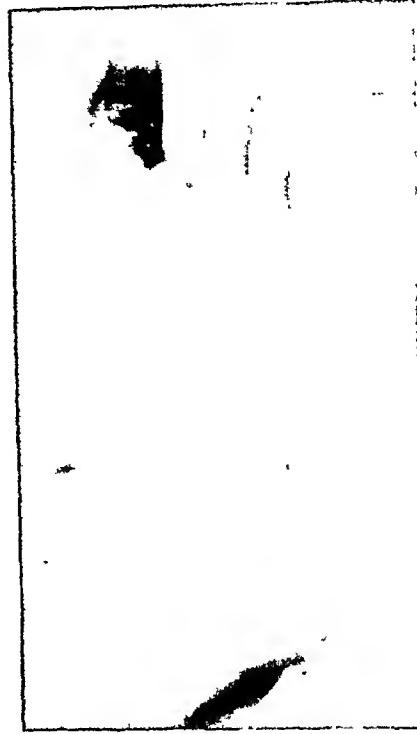


FIG. 10. *Diabetic gangrene:* Although the area of gangrene was relatively small, the marked vascular impairment and the spreading infection necessitated an amputation above the knee as an emergency procedure.

have expressed the belief that it is the act of smoking rather than the actual tobacco that causes vasoconstriction, the fact remains that vasoconstriction results from smoking. While this factor is particularly operative in thrombo-angiitis obliterans, and while in severe occlusive disease the vessels may be able to respond relatively little to the vasoconstrictive impulses, it is obviously advisable in any type of organic vascular lesion, particularly Buerger's disease, to interdict the use of tobacco so as not to interfere with the development of collateralization.

3. *Use of Alcohol.* Wright et al.<sup>156</sup> have emphasized the fact that alcohol has a vasodilating effect. In severe occlusive disease, the vessels may be relatively little influenced by this drug; still it can be empirically used in the hope that a mini-

mum amount, at least, of vasodilatation may occur. The victims of occlusive vascular disease, particularly Buerger's, are



FIG. 11. Arteriosclerotic gangrene: This patient was treated conservatively until it was evident that no improvement in collateral circulation was developing. Amputation was then done at the lowest level commensurate with good healing, which in this case was determined to be above the knee. In the absence of infection or spreading gangrene, conservatism may be temporarily employed in arteriosclerotic gangrene and an elective amputation done when the patient and collateral circulation are in the best possible condition.

impressed with the necessity of "swapping alcohol for tobacco."

**4. Baths.** Various types of hydrotherapeutic measures have been recommended to "massage" the vessels by causing alternate vasoconstriction and vasodilatation, principally the "contrast" baths.

**5. Heat.** Locally, heat has been used to cause vasodilatation, but as has been emphasized already, care must be taken not to use excessive amounts of heat, thus increasing tissue metabolism beyond the available blood supply. Heat has likewise been used in an effort to cause vasodilatation reflexly. Thus Gibbon and Landis<sup>61</sup> have shown that immersion of the forearms in warm water will cause reflex dilatation of the vessels of the lower extremity. Wright recommends the use of the heat pad over the abdomen; deTakats used diathermy to

cause dilatation of the vessels of the lower extremity.

**6. Typhoid Vaccine.** The use of typhoid vaccine to produce vasodilatation was first suggested by Goodman and Gottesman.<sup>63</sup> It has been recommended particularly by Brown,<sup>25</sup> Barker<sup>15</sup> and Wright.<sup>156</sup> Like most of the measures aimed at vasodilatation, this procedure is particularly effective in Buerger's disease because in this disease vasospasm is frequently more evident than in arteriosclerosis. Not being without danger, it is not recommended in the latter disease. Other measures which tend to cause vasodilatation and which are in themselves harmless, may be used even in arteriosclerosis for what value may be obtained.

**7. Hydremic or Pletoric Treatment.** The intravenous administration of saline, particularly hypertonic (5 per cent) and other solutions such as sodium citrate, have been used in order to increase blood viscosity and cause the blood to force its way into the vessels still patent, perhaps recanalizing some that are occluded. Koga<sup>75</sup> first introduced saline infusion for this purpose and it was introduced in this country by Meyer.<sup>106</sup> Silbert<sup>134</sup> introduced the use of 5 per cent saline and has reported excellent results<sup>135,136</sup> with its use, as has Samuels.<sup>126</sup> Saline has largely replaced sodium citrate recommended by Ginsburg<sup>62</sup> and Steel.<sup>144</sup>

**8. Vasodilating Drugs.** Various vasodilating drugs such as nitrites, theobromine, theocalcine, calcium, choline compounds, tissue extract and papaverine have been recommended to increase vasodilatation. While these drugs, particularly papaverine, are of value in acute occlusions, their use in chronic occlusions is not usually productive of marked improvement. While these drugs are of some value in thromboangiitis, they are of very questionable value in arteriosclerosis. But as they are largely harmless, they are frequently used for whatever benefit may accrue.

**9. Mechanical Therapy.** Various mechanical devices have been introduced for the purpose of supposedly developing

collaterals, or the recanalization of occluded vessels. The best known of these devices is the suction-pressure boot, reintroduced by Landis and Gibbon<sup>78</sup> and Herrmann and Reid.<sup>67</sup> Surprisingly good results have been reported by these authors, results which have not been confirmed by most observers. Our observations on the use of this therapy parallels the experience of deTakats.<sup>41</sup> We have used it in a variety of cases and we have found that it is efficacious in relieving rest pain and increasing claudication time in arteriosclerosis, even though no demonstrable changes could be observed by oscillometry or dermal thermometry. We have occasionally observed improvement in non-infected gangrene associated with Buerger's disease, but it has not generally seemed to decrease the area of demarcation. We have found it absolutely worthless in most cases of Buerger's disease and in acute vascular lesions, and its use in infected lesions has been found, as might be anticipated, to spread the infection.

The Sander's "vaso-oscillating bed"<sup>129</sup> has been recommended by Barker and Roth<sup>18,19</sup> and Wright.<sup>156</sup> It acts very similarly to the active exercises of Buerger and Allen, without necessitating any effort on the part of the patient. It is apparently of value in arteriosclerosis obliterans, but is of little value in thrombo-angiitis obliterans.

Reactive hyperemia and intermittent venous occlusion, as recommended by Collens and Wilensky<sup>33</sup> have produced varied clinical results.

**10. Neurosurgery.** In Raynaud's disease, the value of sympathectomy has been well established. Also in Buerger's disease, if it can be demonstrated that vasospasm is present to an appreciable degree, this procedure is likely to increase vascularity to a degree that gangrene may be averted.

As has been pointed out by Smithwick and White,<sup>139</sup> crushing or blocking the nerve supplying a painful toe may not only relieve the pain but it also may, by removing the vasoconstrictor influence, actually increase the available circulation and

improve any local lesion present. Laskey and Silbert<sup>80</sup> have favored sectioning the nerve supply for the same reasons. Relief of pain is an important thing because it permits tolerance by the patient of various other therapeutic measures. Unrelieved pain is, in itself, sometimes the *raison d'être* for an amputation.

In summarizing the prevention of gangrene in extremities with previous vascular disease, it might be said that the principal thing is to avoid trauma, infection or thermal changes which might increase the demands beyond the ability of the available blood supply to satisfy. Particularly in diabetic arteriosclerosis is it important to stabilize the patient and guard against infection. Various vasodilating procedures are of some value in thrombo-angiitis obliterans, as vasospasm is frequently associated, but in arteriosclerosis these procedures are of relatively little value because vasospasm is relatively slight. Various mechanical therapeutic measures give symptomatic relief, particularly in arteriosclerosis, but apparently do little toward producing any *demonstrable* increase in blood supply.

#### TREATMENT OF GANGRENE

Already the question of the treatment of gangrene occurring in limbs free from previous vascular pathology has been briefly discussed. There remains to be discussed gangrene occurring in limbs previously diseased, but we will confine ourselves to cases of thrombo-angiitis obliterans and arteriosclerosis (diabetic and senile) as these comprise the vast majority of cases.

**1. Thrombo-angiitic Gangrene.** In the discussion of gangrene which develops in a limb not previously the site of vascular disturbances, it has been pointed out that because the vessels, other than the one immediately involved, are essentially normal, the collateral forming ability ("blutegefühl") of the limb is excellent. Therefore, it is possible for the area of gangrene to be confined to a relatively small region and amputation anywhere above the demarca-

tion is usually attended with excellent healing. To a lesser degree, this same general idea applies to those cases of gangrene, or impending gangrene, complicating one of inflammatory vascular disease, particularly thrombo-angiitis obliterans. Here the factor of vasospasm frequently plays an important rôle; the vessels are capable of a remarkable amount of re-canalization. Therefore, when gangrene impends, energetic measures aimed at decreasing the vasospasm and increasing the effective circulation should be resorted to. These measures have been enumerated under the methods of conservative therapy (v.s.). But should gangrene actually supervene, frequently it is possible to do a limited amputation and expect healing to occur. Even if a more extensive amputation prove necessary, rarely need it extend above the knee.

As Reid has pointed out, it is no longer satisfactory to classify gangrene and determine the optimum level for amputation: it is necessary to know the actual degree of circulatory embarrassment and to evaluate the rôle of vasomotor nerves, mechanical obstruction, infection and the general condition of the patient. As Finney once said, anybody can amputate a leg, but it takes a good surgeon to save one. By an intelligent study of a case it is possible to do as conservative an amputation as may afford good healing, always bearing in mind the prosthetic necessities.

Allen and Meyerding<sup>6</sup> consider that thrombo-angiitic gangrene extending above the toes is always an indication for amputation, but that "cases of gangrene affecting only the toes in whole or in part should be treated medically provided pain can be relieved and economic conditions permit it." To quote them further: "Amputation of toes may be successful in two types of cases: those in which there is a sudden thrombosis of the vessels of the toes, and those in which either or both of the main pedal vessels pulsate normally, indicating that the vascular occlusion is distal to these areas."

Meleney and Miller<sup>105</sup> recommend, in gangrene associated with thrombo-angiitis, that amputation be below the knee if the popliteal artery is palpable, above the knee if it is not, although they admit that this criterion has not been entirely satisfactory. Perlow<sup>121</sup> recommends oscillometry and dermal thermometry after typhoid injections as means of determining the amount of vasospasm, thus getting an index of the best level of effective circulation, a guide to the best level for amputation.

Horton<sup>70</sup> has pointed out that in cases of thrombo-angiitis receiving little or no treatment, 60 per cent will require amputation within a period of ten years. Wright,<sup>157</sup> on the other hand, has shown that while the amputation rate was 70 per cent in former years, today this has been reduced to from 3 to 10 per cent in some clinics. Certainly with some of the newer therapeutic procedures a more conservative amputation can be done than was formerly thought possible. Amputation should really be considered a "last resort" in thrombo-angiitis. It should be contemplated only for (1) intractable pain, not relieved by conservative measures such as nerve section, (2) a spreading gangrene or one which will show no tendency to heal despite more conservative measures, and (3) infected gangrene which will not localize satisfactorily.

Confronted with a case, however, in which amputation is necessary, two things must be established: (1) the degree of vasospasm present and (2) the level of effective collateral circulation. The larger the element of vasospasm and the lower the level of effective collateral ability, the more conservative can be the procedure, provided the operation is commensurate with a good prosthetic application. Conversely, the less vasospasm present and the higher the demonstrable collateral forming ability of the limb, the higher must be the amputation. A discussion of the methods of determining the degree of vasospasm are beyond the province of this paper, but the methods of determining the level of effective collateral circulation are briefly discussed below.

2. Arteriosclerotic Gangrene. While diabetic (pre-senile) and senile arteriosclerosis are, pathologically, indistinguishable, clinically they present considerably different aspects. Thus arteriosclerosis occurs approximately ten years earlier in the diabetic patient; the operative mortality is nil in senile gangrene but is 3.6 per cent in diabetic gangrene;<sup>52</sup> amputation is more likely to occur and is of more serious import in the diabetic group; major amputations are more often done in the senile than in the diabetic cases.<sup>55</sup>

Despite these general differences, the treatment of arteriosclerotic gangrene is quite similar in the two groups, following certain definite lines, always bearing in mind that in the diabetic group there is a controllable factor which must be treated in addition to the gangrenous process. There are several points of differences between thrombo-angiitic and arteriosclerotic gangrene which should be constantly borne in mind. While not only is the five-year life expectancy following major amputation four times greater in patients with Buerger's disease than in those with arteriosclerosis, major amputations are necessary in far fewer cases of Buerger's disease than in arteriosclerosis.<sup>55</sup> Arteriosclerosis is less responsive to conservative measures because the tissues are older and less resistant to infection, many of the patients are handicapped with diabetes, renal or heart disease, usually larger vessels are blocked in arteriosclerosis and there is less degree of vasospasm present.<sup>157</sup> As a group, arteriosclerotic gangrene has a larger amputation mortality than does amputation in Buerger's disease.

In arteriosclerotic gangrene amputation must be done at some period, and usually it must be more or less radical. The deciding factor as to how quickly the amputation must be done is the question of infection. Obviously, infection is more serious in the diabetic patient because of his increased susceptibilities.

Conservatism is probably justified, as pointed out by Atlas<sup>13</sup> and deTakats<sup>49</sup>

under the following circumstances: (a) gangrene localized to a single toe, (b) the gangrene well demarcated and showing no tendency to spread, (c) no constitutional evidences of toxic absorption, (d) no local evidences of cellulitis or lymphangitis, (e) no intractable pain and (f) response to conservative treatment. Such conservative treatment should consist principally of (a) complete bed rest, with the limb a little lower than the heart, (b) a protective cradle over the foot, *without bulbs*, but with the heat preserved in the part by wrappings, (c) some mild local antiseptic at the area of gangrene, (d) the adequate control of the diabetes if present, as well as general care of the patient and (e) the prophylactic injection of tetanus and gas bacillus antitoxin. Other measures such as vasodilating drugs and mechanical measures may be used, but are of questionable value.

The importance of the preoperative use of tetanus and gas bacillus antitoxin as a prophylactic measure is frequently overlooked. Eliason and his co-workers<sup>53</sup> reported, in 1937, some significant observations regarding the development of gangrene following clean wounds. According to them, Tanner, in 1923, had first reported gas gangrene following amputations through an allegedly clean field. From 1930 to 1937, fifty-two similar cases were reported. Sixty-one per cent of these cases occurred following amputations for diabetic gangrene. At the University of Pennsylvania and Philadelphia General Hospitals, in the period from 1930 to 1935, 6.7 per cent of major amputations (including traumatic cases) developed gas gangrene postoperatively, while Wilson, in Boston, reported an incidence of 2.6 per cent in a series of 420 amputations. In a small series of thirty-six consecutive amputations for either senile or diabetic arteriosclerotic gangrene studied at the Shreveport Charity Hospital, there was one case of gas gangrene developing postoperatively, an incidence of 2.8 per cent.

The mortality varies in this complication but is exceedingly high, particularly in that

following amputation for diabetic gangrene. The interesting fact to be remembered is that in the collected series, the general mortality from the complication of gas gangrene developing after an amputation was 73 per cent in those cases in which no antitoxin was used as compared to a mortality of 51 per cent in which it was used.

At the first sign of spreading gangrene or spreading infection (or if these are present from the start) amputation must be immediately carried out. Once it becomes necessary to amputate, two things must be determined: (1) the level to amputate and (2) the type of amputation to do.

*Determining the Level at Which to Amputate.* The type of amputation will obviously, depend to a certain degree on the level that the amputation can be safely done. It is, therefore, necessary to determine at what level circulation is apparently adequate enough to expect good healing. The old Heidenhain law to the effect that amputation is as a rule best done high as here one is assured of adequate circulation can not be blindly accepted; as while obviously it is true that the higher the amputation the more likely is the circulation to be good, still it has been repeatedly shown that the mortality increases progressively as the level of the amputation becomes higher. One is not justified in carrying out any procedure that carries a higher mortality than is necessary.

The old Moschcowitz test or Matas' modification is still an excellent one, even if frequently forgotten. In essence, the limb is rendered bloodless with an Esmarch bandage; after its removal the limb is watched for the point where the circulation returns rapidly, and this marks the level of effective circulation. The oscillometer and arteriogram are excellent devices to measure directly or visualize the level of efficient circulation. A newer test, and one which is widely used at present, is the histamine test. Eppinger,<sup>54</sup> and later Sir Thomas Lewis<sup>55</sup> showed that the intradermal injection of a small amount of histamine caused

(1) a local dilatation of capillaries, venules and arterioles by direct action with production of a purple spot, (2) a reflex dilatation of surrounding arterioles with production of a *flare* and (3) increase in permeability of the smaller vessels, again by direct action of the histamine, with exudation of fluid into the tissues surrounding the site of injection and the production of a *wheel*. Starr<sup>141,143</sup> and deTakats<sup>38</sup> have adopted this procedure for studying the collateral circulation of an extremity. One-tenth cc. histamine phosphate is injected at several levels. Normally, the reaction to histamine is at its height in five minutes, there being a well developed flare and wheal. Deficient circulation is suggested by (1) delay in appearance of the reaction, (2) poorly developed flare or wheal and (3) failure of flare, wheal or both to appear. The wheal is of more significance than the flare.

There are a number of contradictory reports as to the value of this test. We have found it fairly reliable, although we have experienced difficulty in reading the test in Negroes. Perlow<sup>122</sup> has suggested taking the temperature of the flare in these patients as an index of the degree of reaction. The recent work of Friedlander and associates<sup>125</sup> places some doubt on the reliability of this test. They showed that skin and muscle temperatures and circulation were independent and that the fact that changes occurred in the skin did not mean that they occurred in the deeper structures. Undoubtedly, it is better to ascertain the level of effective circulation before operative procedures are begun. But it should not be forgotten that despite all these tests, if the area in which the operation is done is obviously avascular, the amputation should be done at a higher level.

*Type of Amputation.* Amputations are done chiefly for two reasons: (1) as an *emergency*, life-saving procedure in infection, sepsis, or spreading gangrene and (2) as an *elective* procedure to remove a painful or useless extremity. In general, the type of amputation done will depend on whether or not infection is present and secondly the

level at which the amputation can be safely done, based on a study of the available collaterals. The lower the level of amputation, the lower the mortality, but it must be remembered that rehabilitation will require a useful stump to which an effective prosthesis can be fitted. This not only requires a stump with a good, painless pad, but requires knowledge of the levels at which a successful prosthesis can be fitted. This question has recently been discussed in a series of articles in the *Journal of the American Medical Association*.<sup>11</sup>

*Emergency Amputations in Septic Cases.* Nearly one-half of the hospital deaths from amputations are due to necrosis or sepsis in the amputation stump.<sup>146</sup> Therefore, in most instances, the indications are clear for a circular amputation, usually without closure, at a level at which it can be expected to heal. Secondary amputations to get a good stump may be elected when the patient is in a better general state. This is the general method in which most surgeons handle the question of the septic case. Few follow Zierold's<sup>160</sup> teachings of more or less locally débriding the wound and doing the major amputation later, although in his hands he is able to get fairly good results. Veal<sup>149</sup> believes that the dangers from amputation lie in pulmonary embolism, and he has lately advocated ligation of the femoral vein at the time of amputation to prevent this complication. Experience is too limited to judge the value of this procedure at this time, but it may prove to be a distinct contribution.

In *elective* amputations one has a wider choice of procedures and is guided in his decision by (1) the level of effective circulation and (2) the prosthetic necessities. In summary, it should be remembered that the best sites for amputation, from a prosthetic standpoint are: through the toes, the upper middle third of the leg, the transcondylar region or the middle third of the thigh. Poor sites are through the tarsus or lower third of the leg and just below the knee.

If a localized amputation can be done

through the toes or metatarsals, a good functional result may be obtained without the necessity of any artificial appliance. Of the higher amputations, the Gritti-Stokes has been the most popular, being a lower thigh amputation. Two amputations more recently devised and which are not as generally used or appreciated are the Beverly Smith amputation<sup>137,138</sup> through the leg and the Callander<sup>29</sup> transcondylar amputation. I have seen Dr. Smith demonstrate his amputation and it is a very clever one; it will frequently permit of safer amputation through a lower level than would otherwise be possible. Callander's operation is decidedly the one to do if a higher amputation is required; it carries about one-fourth the mortality of a circular thigh amputation and gives a most excellent functional result. As a general rule, amputations for arteriosclerotic gangrene can seldom be done lower than the mid-third of the leg and usually require amputation in the region of the knee.

#### SUMMARY AND CONCLUSIONS

1. It is important to classify accurately the type of acral gangrene present, as treatment and prognosis vary with the etiology and pathological status.

2. Acral gangrene occurs in two types of cases: (a) those in which there is no previous significant peripheral arterial disease and (b) those in which previous arterial disease has been present.

3. Grouped under those with no previous significant peripheral vascular disease are those due to (a) trauma, (b) thermal changes, (c) embolism, (d) chemicals and drugs, (e) certain forms of thrombosis and (f) local infections.

4. Grouped under those with previous significant peripheral vascular disease are those due to (a) inflammatory disease (e.g., thrombo-angiitis, thrombo-arteritis and syphilis), (b) degenerative disease (e.g., arteriosclerosis, both diabetic and senile) and (c) Raynaud's disease. The physician's responsibility is greater in this

group, for early diagnosis is important in the prevention of gangrene.

5. Certain prophylactic measures in the prevention of gangrene in those without previous significant peripheral vascular disease include protection from trauma, protection from cold, avoidance or careful use of ergot preparations and prevention of stasis in bedridden patients.

6. Active therapy in this group includes principally (a) relief of vasospasm, (b) vein ligation or embolectomy as indicated and (c) local amputations after demarcation.

7. In the prevention of gangrene in cases with peripheral vascular disease the principal thing is an early diagnosis of the disease.

8. If peripheral vascular disease is known to be present, prophylactic measures against gangrene are (a) development of collateral circulation and (b) the avoidance of precipitating factors.

9. Collateral circulation can be particularly developed in diseases with a large amount of vasospasm such as thrombo-angiitis. Collateral forming ability is minimal in arteriosclerosis.

10. Measures used to increase circulation in a limb with peripheral vascular disease include (a) relief of vasospasm by drugs, heat or sympathectomy, (b) hydremic or plethoric treatment, (c) active exercises and (d) mechanical measures including suction-pressure boot, oscillating bed and venous compression.

11. Precipitating factors are principally (a) trauma, (b) infection and (c) thermic changes.

12. In the actual treatment of gangrene one can usually be more conservative or limited in operation in thrombo-angiitis than in arteriosclerosis.

13. The level of amputation will depend on the amount of vasospasm and the level of effective collateral circulation. The more vasospasm and the lower the level of effective collaterals, the lower can be the amputation.

14. The type of amputation done will depend on (a) whether it is an emergency

or elective procedure, (b) the level that amputation is considered most likely to afford healing of the stump and (c) the prosthetic possibilities of the individual case.

15. Two types of amputations are (a) emergency, usually in septic cases, in which the usual procedure is a circular method of amputation and (b) elective, in which the best amputations are (1) through the toes or distal ends of the metatarsals, (2) Smith's mid-leg, (3) Callander's transcondylar and (4) the Gritti-Stokes' supracondylar amputation. The Syme ankle amputation can at times be utilized if a good artificial appliance is obtainable.

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ACCORDING to Bloodgood, infantile hypertrophy of the breasts is due to an ectasia of the ducts of the breast and to their distention with desquamated, degenerated epithelium. The etiology of this epithelial hyperactivity is unknown.

# TRAUMATIC SURGERY

## DISEASES OF THE GENITOURINARY TRACT

E. KING MORGAN, M.D.

Associate Attending Urologist, Long Island College Hospital  
BROOKLYN, NEW YORK

**I**NJURIES to the genitourinary tract, resulting from industrial accidents, are a very small percentage of the total numbers recorded each year. However, it is my belief that the Industrial Labor Commission has to pass on the merits of twice as many claims of injury to the genitourinary tract which are devoid of any descriptive incident or accident involving trauma. The most frequent entity, seen in this atraumatic group, is epididymitis. Many physicians erroneously label these cases as traumatic epididymo-orchitis in their reports, hoping thereby to facilitate the acceptance of the alleged claim. The claimant, many times, is the laboring type, who, through misinformation, associates scrotal swelling with the much used and abused term "strain." He is indignant when told that his swollen testicle is a complication or extension of his kidney, prostatic or urethral infection. Many patients examined for atraumatic epididymitis give the story of the alleged muscular effort taking place on Friday, with the appearance of swelling on Sunday and the subsequent report of the alleged strain being made on Monday. One wonders whether this swelling did not result from the Saturday night social activities. In all these cases a prostatovesiculitis can be demonstrated by smear and culture of the prostatic secretion.

In epididymitis it is important that the treatment not be restricted to local and general rest, plus ointments and hot and cold applications, but it is also necessary to ascertain the initial focus, culture the organism and institute proper chemotherapy in hopes of eradicating the offending organism. Epididymitis is known for its tendency to have acute exacerbations.

Because the external genitals are exposed they are the site of most of the injuries of the genitourinary tract. Injuries to the penis are many and bizarre. Claims of fractured penises have come before the Labor Tribunals. Since the organ has to be in the state of erection in order to be fractured, it is questionable whether industry should be responsible for such an accident. Contusions, hematomas and evulsions of the cutaneous areas are not uncommon and are handled by the usual surgical routine for such injuries.

Recently, a patient received an injury in which the terminal one-fourth inch of the glans penis, to the right of the meatus, was removed as the result of an accident. His subsequent recovery was rapid. However, the tip of the glans, on the uninjured left side, protruded beyond the meatus and was pulled to the opposite side, due to the cicatrix on the right side. This deviation to the right caused the following mechanical interference to the free flow of urine: When the man voided, the stream would strike this obstruction and change its direction to an acute right angle. He claimed disability because of this stream deflection. He refused to have an amputation of the distal one-fourth inch of the glans penis on the unaffected side. Clinically, he was not disabled and had no physical disfigurement visible to the public. Since there was no schedule loss for such an injury he was given a cash settlement to close out the nuisance value.

### TREATMENT

Treatment of penile hematomas, etc., are the same as localized bleeding elsewhere. However, if the bleeding is within the corpora cavernosa the end result is fre-

quently an organized clot, resulting in total or partial priapism. Surgical evacuation of clots promptly relieves this condition.

Lacerations of the penile urethra should receive instant attention by splinting the urethra with an indwelling urethral catheter for forty-eight hours. The end result is always good, if following the accident, the catheter is inserted into the bladder before the patient has voided in order to prevent urinary extravasation by way of the tear. Should the patient have voided before the installation of the catheter, and a phlegmon develop in the penile shaft from the extravasation, the phlegmon should be incised and drained in the manner of a peri-urethral abscess. The prophylactic use of the sulfa drugs is indicated, while the patient wears the indwelling catheter, to prevent or limit a catheter urethritis and prostatitis.

Trauma directly to the scrotum can and does cause rupture of the testicle, hydrocele and hematocoele. These are handled surgically. In addition, the hydrocele can be obliterated successfully by aspiration of the sac and introduction of sclerosing solution.

Torsion of the testicle is an entity which is too frequently missed by the first examining physician who records it by that familiar label "traumatic epididymitis" and treats it as an inflammatory lesion, with the result that the claimant has a long period of unnecessary, painful suffering, with the added loss of time from industry, plus the inevitable useless atrophied testicle. The clinical story is typical: (1) A messenger, riding a motorcycle, runs over a bump, causing him to lose his seat and he sustains immediate pain in the affected testicle, usually accompanied by nausea and vomiting. (2) A busboy, carrying a loaded tray, steps on some spilled food, causing him to slip. He makes a great effort to regain his balance and not drop the loaded tray. He succeeds only to have immediate and continuous pain in the affected testicle. Many more incidents of the same pattern could be cited in which the patients were erroneously treated for

an inflammatory rather than a mechanical lesion. Exquisite tenderness, confined to the scrotum, which defies satisfactory palpation due to extreme pain, plus the typical history, should immediately suggest to the examining physician that he is dealing with an acute torsion, the care of which is surgical and not palliative.

Rupture of the urethra and bladder, either singly or in combination, is frequently seen as part and parcel of crushing injuries in and about the bony pelvis, and it is highly important that the presence of these injuries be determined early and proper measures be taken immediately to short-circuit the urinary outflow before the dreaded urinary extravasation is clinically evident. I make it a rule that all patients with pelvic injuries seen in consultation have an indwelling flexible catheter inserted for forty-eight hours. Failure in catheterization strongly indicates a break in the urethral continuity. If catheterization is successful, the question of ruptured bladder can not be accurately determined by the presence or absence of bladder urine. It is not advisable to introduce per catheter a known quantity of sterile fluid and then measure the return. If the return fluid equals the amount introduced, the deduction is that there is no rupture. However, if the rupture exists, the introduction of fluid causes either a spread in the existing peritonitis or space of Retzius' extravasation, depending upon whether the bladder rupture is intra- or extraperitoneal. The safest method is to introduce one or two ounces of air by means of a sterile syringe, compress the catheter, detach the syringe and place the end of the catheter into a basin filled with fluid, (the basin resting on the mattress, beneath the level of the bladder) and then release the catheter compression. If air bubbles into the fluid with force, the bladder is not ruptured.

There are two reasons for cystotomizing all patients with a ruptured urethra resulting from crushing injuries: First, the rupture is frequently an evulsion of the bladder neck beneath the suprapubic arch. If the

rupture is posterior to the membranous urethra, the extravasation will point into the iliac gutters or space of Retzius and with the suprapubic approach this area will be adequately drained. Second, concomitant bladder rupture may exist which would not be detected from a perineal approach. In addition, secondary repair of a ruptured urethra, if necessary, can be done with greater dispatch if a preliminary cystotomy has been performed, thereby giving the operator a dry perineum.

Kidney injuries divide themselves into two large groups: (1) those cases which result in a perinephritic spill of blood, urine or both and (2) intrarenal injuries, such as subcapsular hematomas and intra-pelvic lacerations with ensuing hematuria. The first group calls for surgical drainage at the earliest opportunity, and nephrectomy if necessary. In the second group, each case is a rule unto itself. Surgery in this group should be the last resort.

Ureteral injuries are a rare entity and are usually associated with perforating injuries to the abdomen. They are always overshadowed by the symptoms resulting from a concomitant ruptured intestinal viscera.

Back injuries are the most costly group from the standpoint of time and medical expense. Every ambulatory patient with an obscure back injury should have a prostatic smear and culture performed. Patients with injured backs requiring long periods of complete immobilization and having associated spinal column and cord injuries, often present an added complication, namely, the so-called orthopedic urinary calculi. The first question raised is whether the calculus antedated the accident or if it is the result of the osteoporosis incident to complete immobilization which causes the mobilization of calcium with attendant hypercalcemia. A decision could be reached more easily if the initial x-ray taken, following the accident, would include detailed films of the kidney areas as well as the spine, and also if frequent urine tests during the patient's inactivity were

recorded. It is a common finding in cases of osteomyelitis of the pelvis and lower extremities that the plates taken cover only these areas, hence, the disputed question of cause and relation of the calculus. It is important that all injuries requiring long periods of inactivity have x-rays made of the kidney areas following such accidents to exclude further controversies.

Apropos of kidney calculi, too many cases of back strain are treated too long before the underlying renal pathological condition manifests itself by hematuria, passage of a calculus or by good medical inspection. The descent of stones from the kidney into the ureter, while at work, causes immediate disability. Does the work initiate the moving of the stone? Many times the Commission has ruled that the replacement cystoscopically of the stone from the ureter back to the kidney pelvis to terminate the pain disability, is all that is required of the employer to discharge his liability if it is proved that the worker was performing tasks that would precipitate the moving of a calculus.

All too frequently are cases recorded of hematuria alleged to be caused by some obscure accident, such as lifting a plank, etc., hours before the initial bloody micturition. Examination discloses the source of bleeding to be from advanced carcinoma of the bladder, an enlarged, engorged prostate or some renal pathological condition such as neoplasm, stone or tuberculosis. By the greatest stretch of the imagination one cannot state that the underlying condition is caused by this lift. Did the lift cause the bleeding? Again, who can say? Bloody micturition is not immediate and, furthermore, these underlying conditions bleed independent of outer body activity because of their progressive destructive nature. The Death Calendar frequently hears claims that have for their premise that death was caused by some trivial accident. The death certificate will give bladder carcinoma and uremia as a cause of death and strenuous attempts are made to prove the facts causally related.

The urological care of the paralyzed bladder resulting from spinal injuries is a very important part of the injured person's treatment. Immediately following the accident closed tidal drainage is the ideal method to be instituted in order to avoid overdistention of the bladder with its attending stasis and infection. This type of treatment is a complicated one and cystometric readings must be made and properly interpreted at frequent intervals so that the manometric pressure of the apparatus may be changed from 2 to 5 mm. of mercury for the atonic cord bladder up to 20 to 30 mm. of mercury for the hypertonic bladder. The important consideration in the care of bladders, whose nerve supply has been interfered with, is to set the organ at rest immediately by an indwelling catheter, and in so doing, use a soft catheter, a No. 14 to 16 French. The larger the catheter, the greater the chances for urethral and prostatic infection. Place the patient, as soon as possible, on a régime of sulfanamides by mouth, plus increased fluid intake. If only the bony portion of the spinal column is involved, this treatment will suffice until the shock and edema have subsided; then micturition will be restored gradually. If

the cord is involved with permanent damage to the bladder nerve supply, tidal drainage is the best method to institute until a so-called cord bladder is established. This end result may be obtained only one to three years after the cord injury.

In industry, the claim of impotence avails naught since one does not have to be potent to make a living. In the state of New York there is no fixed schedule loss for the complete loss or functional derangement of the urological organs. A person losing a toe or finger is awarded a sum fixed by law, not so in the loss or damage to a kidney, testicle, etc. As a result, litigation is protracted.

The world is claim-minded and this applies to the medical profession as well as to the people of industry. Attempts of doctors, under oath, to rationalize that indirect trauma, such as the opening of a drawer of silk stockings, causes nephrophtosis in a thin, long-waisted female, and that orchidectomy performed on a sixty-eight year old man, because of trauma, would six months later cause prostatic hypertrophy with ensuing retention, due to sudden endocrine imbalance as a result of the orchidectomy, is ludicrous, to say the least.



# STONES IN THE DUCTUS CHOLEDOCHUS

AN ANALYSIS OF 2,602 CASES OF BILIARY TRACT DISEASE AT ST. VINCENT'S AND HARLEM HOSPITALS IN THEIR LAST 250,065 HOSPITAL ADMISSIONS

MAURICE CULMER O'SHEA, M.D.

Assistant Surgeon and Chief of Surgical Clinics, St. Vincent's Hospital;  
Associate Surgeon, Harlem Hospital

NEW YORK, NEW YORK

DURING the last decade many changes and considerable progress have been made in the treatment of calculi of the extrahepatic system. This is due primarily to a more complete and better understanding of the problem, derived from experimental research, a finer appreciation of the biochemistry of the liver, and a painstaking analysis of the operative findings and follow-up results of many experienced clinicians and surgeons which has been aided and abetted by cholangiography. In many of the larger hospitals and clinics of the country, it has now become an established routine to investigate the common duct in most cases of cholecystitis, not by palpation alone, but by routine aspiration or by drainage and probing.

Although the criteria for opening the common duct varies with different surgeons, and the advisability of routinely dilating the sphincter of Oddi in cases in which calculi are found is not subscribed to by all, still the majority seem to be of the opinion that cholecystectomy alone will not give sufficiently satisfactory results in all cases, for the same reason that routine cholecystostomies of earlier years failed, namely, because there was left behind in the ducts either calculi, or infection, or both. More radical investigation and surgery than were usually attempted in the past is now believed to be essential and necessary.

The technic of the surgical procedures has been well espoused and illustrated in the literature of the last few years so I will touch only lightly upon it. However, in this article I am endeavoring first, to emphasize

the recently recognized high incidence of stones in the common and hepatic ducts in cases which have been hospitalized and operated upon for acute or chronic cholecystitis or pancreatitis, and, secondly to clarify, as simply as possible, the indications as to what type of surgery should be attempted and when it should be undertaken. Thirdly, I present an analysis of 2,602 cases of biliary tract disease at St. Vincent's and Harlem Hospitals among their last quarter of a million hospital admissions from 1931 to 1941. Lastly, I present a case report of a patient in which a common duct stone or stones were not found at the time of operation, but which were subsequently passed spontaneously after the administration of certain medications which are advantageous in stimulating normal function of the biliary system.

No matter what the criteria of the surgeon may be, he always should be conscious of the danger, the possibility, and even the probability, of the existence of a stone in the common or hepatic bile ducts whenever an operation for gallbladder disease is attempted. To overlook such a stone may result in failure of relief from symptoms, or may even prove fatal.

## INDICATIONS

The question of what indications should guide a surgeon in his judgment as to the advisability of routinely exploring the ducts in cases of cholelithiasis and cholecystitis differs in many minds. I will enumerate a few of their criteria:

Bettman and Tannebaum<sup>4</sup> reported that their experiences at Michael Reese Hospital have led them to believe that a common duct should never be opened unless it is

markedly dilated, a stone palpated or the icteric index has remained high at time of operation in a case with a previous history of jaundice.

Frank H. Lahey<sup>19</sup> has urged that at the time of operation for gallstones not only a cholecystectomy be performed but that the common and hepatic bile ducts be explored in all cases in which the common duct was dilated, the head of the pancreas thickened, the gallbladder thickened or contracted or a stone palpated, and when an aspirated common duct contains dark cloudy, or murky bile. Jaundice is not believed by him<sup>18</sup> to be a reliable sign of the existence of a common duct stone, for he found that jaundice was present in only 60 per cent of the cases in which he removed a common duct stone, while Judd<sup>20</sup> reports the existence of jaundice in only 73.4 per cent of his cases. Jaundice is usually a late sign that occurs after considerable liver damage has taken place.

It is the opinion of Graham<sup>10</sup> that if after restoring the biochemical balance there is undiminished pain, despite adequate sedation, or if the pulse rises, or remains persistently high, direct surgical attack is indicated, in cases of cholecystitis.

Beall<sup>3</sup> expressed himself to the effect that the great majority of the cases of stone in the common duct are not in need of emergency surgery, and he emphasizes the great preoperative value of fluids, sugar, intravenous calcium and transfusions.

Heyd and Hotz<sup>13</sup> emphasize that a pathological condition of common duct is usually secondary to that of gallbladder. They further urge that to prevent such a condition of the common duct early diagnosis and operation is necessary on the gallbladder. Lahey, Walters, and others agree with them on this subject.

Whipple<sup>33</sup> holds that in long standing chronic cholecystitis, acute obstruction and infection of the common duct, the duct should be opened and drained, for such obstruction may be due to a stone in the common duct or to a pancreatic lymphangiitis. If an acute cholangitis is present with

an acute cholecystitis, the indications for drainage of the common duct are more urgent than if just an acute cholecystitis were present. He asserts that acute attacks of gallbladder disease are often accelerated in the already diseased gallbladder by progressive common duct obstruction from calculi or neoplasms and by, or together with, the resultant circulatory changes in the walls of the diseased gallbladder. The attitude in the past of certain physicians that surgery should be resorted to only after jaundice and sepsis have failed to respond to internal medication is decried as erroneous. The axiom that it is unwise to perform extensive abdominal exploration in the presence of an acute or suppurative lesion within the peritoneal cavity is in need of modification when it is applied to surgery of the biliary tree. When one reviews a large series of cases and the literature on acute cholecystitis and observes how often, because of improper exploration, serious underlying disease in the common bile ducts is overlooked, this proverb becomes all the more improper, erroneous and outmoded.

Thus it may be said that in cases in which cholangitis exists, a stone is palpated, the common duct is dilated, murky bile is found upon aspiration or jaundice is present, it becomes urgent for the surgeon to open, probe and drain the common duct in any case of cholelithiasis and cholecystitis. To these indications, some would add those cases of chronic and acute pancreatitis because of the usual co-existing infection and the presence of calculi in the biliary ducts. Surgery in these cases should not be hasty nor should it be delayed, but rather attempted at the first opportune time when the patient's fluid and biochemical balance have been re-established.

#### INCIDENCE

The high percentage of stones in the common duct in cases of cholecystitis and pancreatitis is emphasized by many authors and surgeons during the past few years. Although the incidence of cholelithiasis as

found by all is fairly uniform, the percentage of stones found in the common duct varies greatly, and in proportion to the number of common ducts that are explored and drained routinely whenever any of the aforementioned indications are present.

Among the negro race, gallbladder disease is usually rare, this in spite of their dietary delights of fried foods and their frequently unbalanced or impoverished diets. However small the incidence of cholecytic disease, it is amazing to observe in young negroes, the occurrence of gallstones in a high percentage of the patients who are suffering from the hereditary condition of sickle cell anemia. At Harlem Hospital where between 70 and 80 per cent of the patients are of the negro race, only 604 of the 154,908 patients admitted in the past ten years were diagnosed as suffering from disease of the biliary tract, and the majority of these 600 were white people. The percentage of these cases at this hospital who had cholelithiasis was 35.3 per cent, and of these 5.9 per cent (twelve cases) had stones in the common duct, 6.8 per cent of the total operative cases had a choledochal calculus, while the common duct was explored surgically in only 8.5 per cent of the cases. In addition to obstruction of the duct by calculi, one patient was diagnosed as having his common duct obstructed by laboratory proved parasites of the *Strongyloides stercoralis* species. At Harlem Hospital less than four-tenths of 1 per cent of all hospital admissions were found to have complaints referable to their extrahepatic system, and the percentage for those of the negro race was even lower, about one-tenth of 1 per cent of all admissions. (Table I.)

At St. Vincent's Hospital during the past decade, 95,157 patients were admitted and of these 1,998 were found to be suffering from disease of their biliary tracts. Thus about 2 per cent of the total admissions had irregularities of their extrahepatic systems. Of 1,971 cases of cholecytis, 998 cases, or 51 per cent had biliary calculi and eighty-nine patients, or 4.6 per cent, had calculi in the hepatic or common ducts.

TABLE I  
ANALYSIS OF INCIDENCE AND COMPLICATIONS

	St. Vin- cent's Hos- pital	Harlem Hos- pital	Both Hos- pitals
Cases of acute cholecystitis (including empyema) (gangrene, suppurative)	449	260	709
Cases of chronic cholecystitis (including hydrops)	1,532	317	1,849
Total cases of cholecystitis	1,971	577	2,548
Total operative cases of cholecystitis	1,438	137	1,575
Cases of acute cholecystitis with cholelithiasis	243	73	316
Cases of chronic cholecystitis with cholelithiasis	758	130	888
Total cases of cholecystitis with cholelithiasis	1,001	203	1,204
Cases with calculi in ductus choledochus	83	12	95
Cases with calculi in ductus hepaticus	6	0	6
Total cases calculi in the extrahepatic ducts	89	12	101
Percentage of cases of cholelithiasis	51%	35.3%	47.2%
Percentage of cases of cholelithiasis with common duct stones	5.7%	6.8%	6.2%
Percentage of operative cases of cholelithiasis with common duct stones	5.3%	7.3%	5.5%
Percentage of common duct drainage	6.4%	8.5%	6.6%
Percentage of common duct drainage where stones were present	82.8%	86%	82.9%
Obstruction of common duct by parasites	0	1	1
Obstruction of common duct by stricture	3	0	3
Cases of cholangitis (acute)	45	7	52
Cases of pancreatitis	51	0	51
Cases of intestinal obstruction	2	0	2
Cases of cholecystoduodenal fistulas	2	0	2
Cases of external biliary fistulas	12	0	12
Cases of adenocarcinoma of gallbladder	0	4	4
Cases of stab wounds or perforation of gallbladder	0	3	3
Total cases of disease of extrahepatic system	1,998	604	2,602

Of those 998 cases of cholelithiasis, 9 per cent had common duct calculi. The common duct was explored surgically in 7.7 per cent of the 1,438 cases in which the patients were operated upon, and in these 5.7 per cent were found to have common duct stones.

troubled by embarrassing adhesions about the gallbladder. In addition there were fifty-two cases of cholangitis, only twenty-two of which apparently were not associated with calculi of the common duct or disease of the gallbladder. Seven patients had cholecystostogastrostomies performed.

TABLE II

SHOWING COMPARATIVE STATISTICS OF OVER 9,272 CASES OF CHOLECYSTITIS. THE PERCENTAGE INCIDENCE OF COMMON DUCT STONES INCREASES WITH THE PERCENTAGE OF CASES THAT HAVE THE COMMON DUCT DRAINED

Hospital Series, Author and Reference	Operative Cases of Cholecystitis	Per Cent with Cholelithiasis	Per Cent Common Duct Drainage	Per Cent Common Duct Stones	Per Cent Calculi in Drained Ducts
St Vincent's Hospital, New York (1930-1940)	1,438	51	6.4	5.3	82.8
Harlem Hospital, New York (1930-1940)	137	35.3	8.5	7.3	86
Combining St Vincent's and Harlem Hospitals (1930-1940)	1,575	47.2	6.6	5.5	82.6
Post graduate Hospital, New York, <sup>12 13</sup> Hcyd and Hotz (1920-1937)	3,306	60	7.7	6.3	86
Vicksburg Hospital, Mississippi, Willard Parsons <sup>22</sup>	X	X	16	15	94
Lahey Clinic, Boston, Frank Lahey <sup>17 18</sup> (1910-1925)	619	X	15	8.4	54.2
Lahey Clinic, Boston Frank Lahey <sup>17 18</sup> (1925-1935)	1,158	X	37.5	16.8	44.7
Massachusetts General Hospital, Boston, Allen and Wallace <sup>2</sup> (1930-1935)	1,228	X	32	13	42
Massachusetts General Hospital, Boston, Allen and Wallace <sup>2</sup> (1935-1940)	860	X	44.2	20.7	46.8
Peter Bent Brigham Hospital, Boston, David Chevers <sup>8</sup> (1913-1935)	426	44	37.9	16.7	44.3
P L Mirizzi, Argentina <sup>21</sup>	100	X	44.2	23	52
Post-Graduate Hospital, New York, Carter and Hotz <sup>7</sup> (1920-1937)	3,306	Pancreatitis cases 53	{ Acute Chronic	.78 .66	

Combining the cases of the two hospitals we find that in ten years 250,065 patients were admitted. Of these 2,548 had cholecystitis and 1,204 of these had biliary calculi, that is, 47.2 per cent. There were 101 patients (4 per cent) with stones in their common or hepatic ducts, ninety-five being in the common duct and six in the hepatic ducts, and one case with obstruction caused by the *Strongyloides stercoralis*. Three patients had penetrating stab wounds of the gallbladder and four are reported as suffering from adenocarcinoma of the gallbladder. Twelve patients had external biliary fistulas after previous surgery and two were found to have spontaneous duodenal biliary fistulas. Ten were

Of the 101 stones found in the ducts of the extrahepatic system, one of the six hepatic duct stones and four of the ninety-five cases of common duct stones had the calculi discovered at autopsies. Of the remaining ninety-six cases, stones were removed at eighty-seven operations and the remaining nine cases had the presence of the stones in the common duct proved by x-rays and clinical signs, with the patient refusing surgery. Of a total of 1,855 cases of cholecystitis in which the patients were operated upon at Harlem and St. Vincent's Hospitals, common duct stones were found in 6.2 per cent and the ducts were drained in 7.7 per cent of the patients. (Table II.)

Recently, Lahey<sup>19</sup> has explored the ducts in over 40 per cent of his operative cases, and has found stones in the common or hepatic ducts in nearly 20 per cent of these cases. Stones were found in 323 of the 718 cases in which he opened the ducts and in spite of the additional surgery of common duct drainage by a "T" tube, his morbidity and mortality diminished. A somewhat similar high percentage of calculi in the ducts was found by P. L. Mirizzi of Argentina<sup>21</sup> who reported that in his last 100 operative gallbladder cases 23 per cent had common duct calculi and one of calculus in the hepatic duct. Cheever<sup>8</sup> found stones in the gallbladder in 44 per cent of the 426 cases of gallbladder disease operated upon by him. Allen and Wallace<sup>2</sup> found common duct stones in only 13 per cent of their 1,228 cases and they explored 32 per cent of them. Heyd and Hotz<sup>13</sup> reported exploring 7.7 per cent common ducts in a series of 3,306 cases of cholecystitis and finding stones in 6.3 per cent cases. This incidence is quite similar to ours.

In a series of cases of pancreatitis reported by Carter and Hotz<sup>7</sup> common duct stones were found to be present in 66 per cent of the cases that had biliary tract disease and chronic pancreatitis and in 78 per cent of those with acute pancreatitis. They further noted that in all their cases of either chronic or acute pancreatitis on whom biliary tract surgery was performed all but 6 per cent of their cases showed biliary tract disease.

Aside from the danger of a stone in the choledochus and the existence of a pancreatitis, another important reason for exploring and probing the common duct in cases of acute cholecystitis is the lurking danger of the possibility of carcinoma of the ducts or the head of the pancreas. Rothenberg and Aronson<sup>28</sup> report eight recent cases of patients who were operated upon for cholecystitis in whom within three days to twelve weeks later they manifested signs that were later verified by either biopsy or autopsy as carcinoma of either the ducts or the head of the pancreas. In no

one of these cases did the surgeon realize the existence of malignancy because of the acuteness of the gallbladder inflammation and the fact that seven of the eight had pain similar to that of biliary colic. In two of the cases carcinoma was suspected pre-operatively but not verified at operation.

#### TREATMENT

Before any surgery is attempted in these cases, it is important to fortify these patients with intravenous fluids that will re-establish their normal biochemical and electrolyte balance, and when possible vitamin K and bile salts should be administered in ample dosage.

When enumerating a few of the important steps in the surgical procedure to be followed when exploration of the common duct is decided upon, it might be stated that many advocate when possible to drain through the stump of the cystic duct after incising its distal wall and extending the incision about one-quarter of an inch along the common duct, and then further exploring with the probe and scooping out any stones or gravel. The exploration should be carried out proximally as well as distally, for often calcareous materials will be found in the common hepatic or hepatic ducts. Drainage with a catheter down to or extending through the sphincter of Oddi or drainage of the common duct with a "T" tube of Deaver are all procedures advocated by various surgeons. The duct should be sutured securely about the inserted drain. If the patient's condition is extremely critical at time of operation, it may be advisable to drain the common duct away from its anastomosis with the cystic duct and leave the gallbladder for removal at a subsequent operation, or else to drain the gallbladder in addition, if circumstances permit.

Beall<sup>3</sup> who differs with most of the expressed opinions on the subject of drainage, believes that the common duct after being explored should be sutured so as to prevent the deleterious effect on the body of the loss of bile, which is manifested by a

loss of calcium and poor fat digestion. His technic is to close the incision in the duct and then drain down to it.

Routine aspiration of the common duct with an aspirating syringe is advocated by Lahey<sup>19</sup> for all cases of cholecystitis in which there is any suspicion about the contents of the duct. If the aspirated bile is cloudy or murky and has lost its golden glow, he recommends that the common duct be incised and drained. Such bile usually is infected and the probability is that some infection is present in the walls of the ducts.

Slow dilatation of the papilla of Vater is not only a safe procedure, but advisable following common duct exploration according to the work of Allen and Wallace.<sup>1</sup> This dilatation does not predispose to ascending infection nor does it seem to be permanent, or cause any cicatricial constriction. Although their cases showed an increase in the percentage of pulmonary complications, other complications were fewer and the drainage time was shorter. At one time all postoperative biliary colic following cholecystectomy was attributed to spasm of the sphincter of Oddi; however, such postoperative biliary colic is now believed to be the result of stones and gravel in the common duct or pancreatitis with a resultant spasm of the sphincter.

The high incidence of stones in the ducts as found by surgeons during their more thorough investigations of recent years leads one to assume that postoperative colic is caused by retained calculi. It is the rare case in which abnormal function of the sphincter of Oddi occurs alone as biliary dyskinesia.

If after removal of stones from the common duct and its subsequent drainage a choledochogram is performed either routinely or for failure of the relief of pain, and another stone is demonstrated, Walters, Butsch and McGowan<sup>5,20</sup> recommend using the technic of Pribram<sup>25</sup> or Osterberg, of injecting ether, or ether diluted with alcohol, followed by liquid paraffin, through the drainage tube into the common duct.

By this method the retained stone may be partly dissolved and sufficiently fragmented so that it may be forced through the sphincter of Oddi when pressure is dammed up in the duct by temporarily clamping off the drainage tube. Further relaxation of the sphincter may be induced by amyl-nitrate inhalations or placing nitro-glycerine tablets beneath the tongue. Recently, I have had an opportunity to observe at St. Vincent's Hospital just such a case of a retained common duct stone that was partly dissolved by ether and alcohol injected through a drainage tube in the common duct and subsequently passed into the intestines. The same authors, Walters, Butsch and McGowan<sup>5</sup> have demonstrated that the normal intraductal pressure was 0 to 30 mm. of water, but that during attacks of biliary colic, the intraductal pressure frequently went as high as 160 mm. The use of opiates, especially morphine, tend to increase the intraductal pressure.

The use of sulfanilamide powder or any of its kindred preparations within the wound and especially about the drainage area of the common duct is recommended and urged. About 12 to 15 Gm. within the abdomen and about 3 to 4 Gm. scattered in the closure of the layers of the abdominal wall have been found to decrease the incidence of peritonitis and wound infections and predispose to a more uneventful recovery. The absorption of the drug from these areas seems to be relatively slow, for seldom was the Marshal test recording appreciably elevated.

#### COMPLICATIONS

After omitting all cases of catarrhal jaundice and its co-existing cholangitis, fifty-two cases of cholangitis were found to be present in this series of cases, and of these twelve died and twenty-three were operated upon. The remaining patients either refused operation or were treated by duodenal drainage, or symptomatically with surprisingly good results. The majority of these cases were associated with

cholelithiasis and cholecystitis. Various degrees of hepatitis, jaundice and biliary cirrhosis was recorded in many of the cases

tractions caused by previously impacted common duct stones may cause as great or greater trouble in the future than the



FIG. 1. Large gallstone in loop of small intestines in pelvis causing complete intestinal obstruction.

and fifty-one of the patients were found at the time of operation to be suffering from some degree of pancreatitis. Twelve cases of persistent external and two of duodenal-biliary fistulas have already been enumerated in the analysis of this series of cases.

Strictures, as a result of cicatricial con-

stones caused. Strictures also occasionally form at the site of exit of the "T" tube from the duct.

Impacted stones in the ampulla of Vater not infrequently cause pancreatitis as they either plug off drainage from the pancreatic duct of Wirsung or else dam up the

contaminated bile in the common duct and cause an overflow into the pancreas through its main duct.

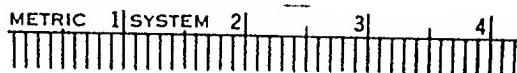


FIG. 2. Stone removed from small intestines at enterotomy.

Occasionally, gallstones of great size are passed through the ampulla or else through a fistulous tract between the gallbladder and the duodenum and cause a resultant intestinal obstruction. This obstruction occurs usually in the ileum or at the ileocecal valve and more rarely in the jejunum or the colon. One such patient with an obstruction of the ileum of long duration was operated upon by us two years ago. A short summary of the case with illustrations of the obstructing stone is presented (Figs. 1, 2 and 3):

#### CASE REPORT

A. L., aged sixty-two, a white female, was admitted to St. Vincent's Hospital by ambulance on August 19, 1939, complaining of sharp, cramp-like right upper quadrant pain, which radiated to her back, and was accompanied by nausea and vomiting. This present attack started four days before admission, but a similar attack associated with increasing weakness, an unproductive cough and alternating constipation and loose bowel movements manifested itself two weeks prior to admission. Her past history was negative except for dyspnea on exertion for the past two years.

On physical examination the temperature was  $104^{\circ}\text{F}$ ., the pulse 126, blood pressure 140/86 and respirations 24. The patient was greatly

dehydrated, and appeared acutely ill and very weak. No dyspnea and no jaundice were present. There were râles in both bases with

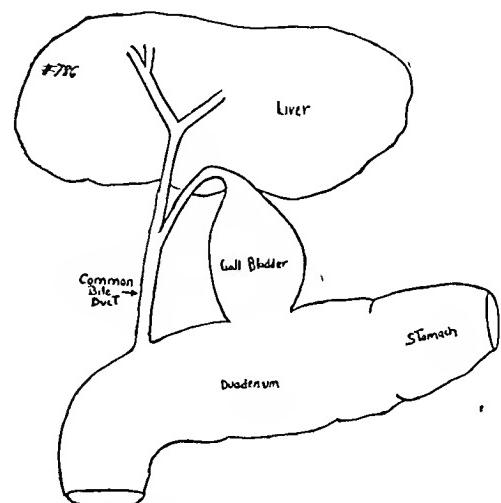


FIG. 3. Illustrates spontaneous cholecysto-duodenal fistula through which gallstone entered intestines.

dullness and diminished breath sounds in the right lower lobe. The heart was slightly enlarged, was of regular rhythm and no murmurs were audible. The abdomen was distended and revealed no scars. There were no areas of tenderness and no palpable masses but there was shifting dullness in the flanks. Rectal and vaginal examinations were negative and there was no edema of the extremities.

Laboratory analyses of the urine disclosed a trace of albumen, and an occasional red blood cell and white blood cell. The red blood count was 5,000,000, the hemoglobin 94 per cent (13.5 Gm.), the white blood count was 7,160 and there were 86 per cent polymorphonuclear neutrophiles, 12 per cent lymphocytes and 2 per cent myelocytes. A blood culture taken a few hours after admission was negative.

X-ray examination of the abdomen revealed a large collection of gas in distended loops of the small intestine, particularly on the left side. There was a calcified mass in the left pelvic fossa which was below the level of the distended coils of intestines. This mass was believed to represent either a gallstone or a fecalith.

*Diagnoses:* Intestinal obstruction (small intestines), bronchopneumonia and arteriosclerosis. Operation was delayed long enough to attempt to re-establish her fluid and electrolyte

balance by intravenous medication and to decompress her distention by Wangensteen drainage.



FIG. 4. X-ray taken in original hospital prior to removal of gallbladder and stones in gallbladder and stone in the ampulla of Vater.

The abdomen was opened by a right rectus incision and no free fluid was found to be present. The small intestines were greatly distended and eighteen inches above the ileocecal junction a large spool-shaped mass was found to be impacted in the ileum and to be the cause of the complete obstruction. The mass could not be milked backward and was removed from the intestines by an enterotomy, and found to be a large gallstone which measured 4 by  $2\frac{1}{2}$  cm. The abdomen contained many adhesions in the right upper quadrant and the gallbladder could not be visualized. The abdomen was closed without drainage.

The patient died on August 20, 1941, twelve hours after operation. At autopsy no evidence of any leakage about the site of the enterostomy was found to be present, but a spontaneous cholecystoduodenal fistula with a large lumen existed. The cause of her death was believed to be overwhelming toxicity from an intestinal obstruction of four days' duration and her bronchopneumonia.

The following case history is one of a type that occurs all too often, namely, retained common duct stones after chole-

cystectomy. This particular patient had the good fortune to pass her stones into her intestines and avoid the hazardous experience of a second operation on her biliary system.



FIG. 5. Showing stone in ampulla of Vater that was not discovered at time of operation.

ence of a second operation on her biliary system.

Mrs. V. B., a fifty-year old white lady was taken ill about March 1, 1939, at her home. She complained of pain and a marked soreness in her midepigastrium which were greatly accentuated when she stood upright. The pain radiated at times to both scapular areas and was occasionally accompanied by nausea and vomiting. After four weeks of symptomatic treatment with diet and sedatives by her local doctor, surgery was decided upon and she was hospitalized. Preoperative x-rays taken at that hospital revealed the presence of a large stone 2 cm. in diameter, and a smaller stone about 1 cm. in diameter in the area of her gallbladder. (Fig. 4.) However, there was a third stone visible in the x-ray at the level of the transverse process of the third lumbar vertebra that apparently escaped their attention. On April 4, 1939, she was operated upon and a huge hydrops of her gallbladder showing signs of ulceration and containing many stones was found. A cholecystectomy and an appendectomy were performed, and the operation report stated, "there were no stones in the common duct." The duct, however, was not opened and probed.

The patient states that following operation she never obtained complete relief from her "soreness in the epigastrium," but her wound

this time she was markedly dehydrated, jaundiced and in severe pain. This pain radiated from her midepigastrium to her back and her

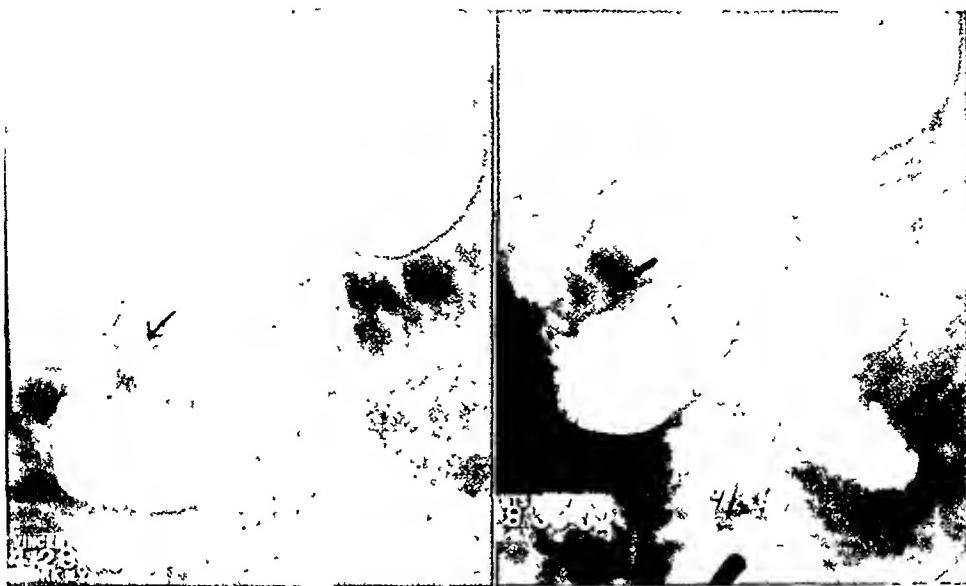


FIG. 6.

FIG. 7.



FIG. 8.

FIGS. 6, 7 AND 8. Illustrate relation of stone in common duct to the duodenum after administration of a bismuth meal.

healed well and she was discharged from the hospital on her twelfth postoperative day. She subsequently moved to New York City where she was first seen by me on April 24, 1939, about three weeks after her operation and a diagnosis of common duct stone was made. At

two scapular areas. She was admitted to St. Vincent's Hospital the following day, April 25, 1939.

At this time, the patient's jaundice, distress and pain had increased and her stools were light in color. The urine was amber in color and

positive for bilirubin and urobilinogen in dilutions of 1:10 but negative in dilutions of 1:20. Laboratory analyses of her blood revealed

ported as having existed in her massive gall-bladder. Consequently, it was decided to make an attempt with the aid of certain medication



FIG. 9.



FIG. 10.

FIGS. 9 AND 10. Illustrate stone in cecum after passing from the ampulla of Vater through the small intestines.

the following: (1) The red blood count was 3,630,000 with 78 per cent hemoglobin; (2) the white blood count was 11,750 with 87 per cent polymorphonuclears and a slight shift to the left; (3) her blood was type IV; (4) the blood sugar was 90 mg. and the nonprotein nitrogen was 27; (5) the icteric index was 43; (6) the Van den Burgh was 3-plus biphasic indirect (being 10 mg.). Flat x-rays of the abdomen revealed the presence of a rounded opaque body at the level of the right transverse process of the third lumbar vertebra. Confirmatory x-rays taken after ingestion of a barium meal again showed the rounded opaque body to occupy a position corresponding to the location of the ampulla of Vater. (Figs. 5 to 8.)

The positive findings of these x-rays, the elevated icteric index, the jaundice, and the persistence of pain across both low scapular areas and the midepigastrium, together with her nausea and vomiting confirmed the admission diagnosis of common duct stone following a cholecystectomy.

The method of treatment then had to be determined. The patient had been suffering marked pain for nearly two months and operation had given her little or no relief. She had lost her desire to live, was asthenic, a mild cardiac, dehydrated, and in the past several weeks had lost twenty pounds in weight. In brief, in her present condition she was only a fair surgical risk and if operation were to be performed considerable adhesions were to be expected because of the gangrenous areas re-

to encourage the spontaneous passage of the stone. Accordingly, the following régime was instituted on April 29th: (1) bile salts gr. 10, three times a day with meals; (2) fatty meal at noon each day; (3) precede each fatty meal with atropine gr.  $\frac{1}{150}$  (by hypo); (4) nitroglycerine gr.  $\frac{1}{100}$  three times a day before meals; (5) allow patient up in chair; (6) no morphine unless pain is too severe to tolerate.

Atropine and nitroglycerine were administered in an effort to relax the obstructing contraction of the smooth muscle fibers in the duct and the sphincter of Oddi at the ampulla of vater. Nitroglycerine tends to relax or inhibit smooth muscle tissue directly, while atropine, a useful anodyne in gallstone colic acts on the nerve ends of the vagus nerve which supplies motor fibers to the biliary tract musculature and inhibitory impulses to the sphincter of Oddi permitting it to dilate. The "fatty meal" was given so that, whatever stimulation the duodenal hormone, "cholecystokinin," might exert on the biliary tract after the removal of the gallbladder, would be utilized to help evacuate the stone. Morphine was not prescribed except as a possible necessary analgesic because of its inhibiting effect on the rhythmic contractions of smooth muscles.

The efforts of the first day were unsuccessful, but on the second day the patient experienced an increase in her pain, an elevation of her temperature to (100.6°F.) and her pulse rate which previously had been between 70 to 80 rose to 100. Shortly thereafter the acute pain

in her epigastrium subsided and was replaced by a soreness while the pain in both scapular areas disappeared entirely. A check-up flat

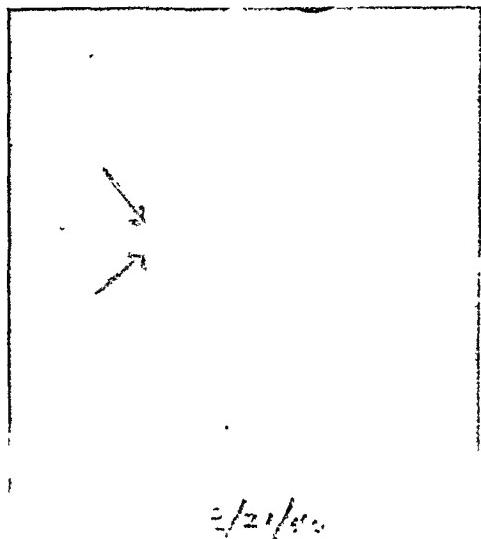


FIG. 11. Shows the presence of a new stone in the common duct one year later.

X-ray of the abdomen taken on May 1 and repeated the following day showed the stone to have passed into the large intestines. (Figs. 9 and 10.)

During the following days, the patient's clinical jaundice subsided, her icteric index fell to 19 on May 3, and all her pains and nausea disappeared. Her stools became brown in color, but the stone was not recovered from them. The patient was discharged from the hospital as cured on her twelfth hospital day. She was symptom free for the following seven months.

On January 15, 1940, she again appeared at my office complaining of occasional nausea and a return of pain in her midepigastrium which pain radiated to her right flank and scapular area and less so to her left flank and scapula. This pain seemed to her to be different in character to her previous pains. The pain had manifested itself on only five or six occasions in the past three weeks, and she attributed it to having eaten too heavily during the Christmas and New Year holiday season. Although she had gained two pounds in weight, she felt generally poor and had been troubled with sluggish bowels and abdominal distention, which was not accompanied by either belching or the passing of flatus. X-rays of the stomach and intestines revealed no pathological condition but did reveal a dense shadow in the right

side of the abdomen that was believed to represent a moderately enlarged right hepatic lobe. The suspicions of the existence of an ulcer unconfirmed, the possibility of a recurrence of the chronic pancreatitis which she was reported as suffering from at time of operation was considered and an analysis of her blood showed the "amylase" content to be 182 units (normal 70 to 200) and the urine amylase to be 170 units, also within normal range. Her pain for forty-eight hours after the gastrointestinal series was unrelenting. She was nauseated and vomited. Her temperature and blood count were relatively normal and her icteric index was 7.5. Multiple X-rays taken of the "biliary tree" (flat plates and a keraphen series) failed to disclose any evidence of a calculus or a distended common duct. However, the colon enema series that revealed a mild colitis, did reveal evidence in one film that was strongly indicative of a new common duct stone. This shadow was located exactly where her previous common duct stone shadow was located at the tip of the right transverse process of the third lumbar vertebra. (Fig. 11.)

This second stone although smooth, oval and apparently solitary, cast a different type of shadow from the stone of a year ago. This second stone's shadow was "signet ring" in type and probably was formed by deposition of layers of cholesterol, pigment calcium and calcium carbonates. The shadow cast in the films of the previous solitary stone although also oval and smooth, was solid and dense, and was probably a so-called "combined calculus" formed by a radial cholesterol calculus with a laminated cholesterol calcium covering.<sup>33</sup>

Since this shadow of a stone was not present after her attack subsided several months ago, and since the patient has been entirely well and symptom free for the seven months prior to January of this year, it is interesting to speculate where the stone was formed. Did it form in a branch of the right hepatic duct and cause the resultant swelling of the right lobe of the liver, or could there have been a spasm of the sphincter of Oddi in the ampulla with a resultant stasis and dilation of the common duct with bile elements and infection piling up a new stone? The latter of the two is more probable. As the patient was free from signs of a clinical jaundice, the icteric index was low and the pain was irregular in time and duration, it was probable that this stone was not wedged in the

ampulla like the previous stone, but rather was acting like a ball valve. The patient requested that surgical intervention be postponed until after another attempt had been made to pass the stone with the aid of medication. A trial period of medication as previously described was instituted and following this the patient was unusually free from pain and felt better for four days.

However, on the fifth day, the patient was suddenly seized with a very severe attack of pain in her right upper quadrant and mid-epigastrium that prostrated her. This pain radiated to both her back and right scapular area and was relieved only after the administration of morphine and atropine hyperdermically. The acute pain disappeared within a few hours just as suddenly as it had come. During the following twenty-four hours the patient had a mild degree of soreness in her epigastrium, and on the following day she was discharged from the hospital symptom free.

In the month following her discharge from the hospital she gained twelve pounds in weight. Her medication of bile salts was continued, her diet was only slightly restricted and the enlarged right lobe of the liver shrunk in size. She was observed by me at frequent intervals for a year after her discharge and she had no recurrence of her previous acute distress and vomiting.

It is too much to expect that all such cases could have such a successful and non-surgical ending, but in this case and in two other cases that have since come under my observation, patients have successfully passed a retained common duct stone after instituting this method of treatment. However successful this method may be in some cases in assisting in the passage of a common duct stone, it must be borne in mind, that some degree of infection of the bile in the duct usually exists wherever a stone is present, and that this method does little to improve the infection.

#### CONCLUSIONS

- Common duct stones are very frequently present in cases of cholecystitis and pancreatitis and should be carefully searched for. The high incidence of chole-

dochol stones is substantiated by findings in a review of the recent literature.

- Criteria for drainage of the common duct are, the presence of infection or stones in the duct, dilatation of the duct, the aspiration of murky bile from the duct, or the existence of pancreatitis or jaundice, together with a persistent high pulse rate in spite of adequate sedation. To these most surgeons would also add a small contracted gallbladder or multiple small stones within it.

- Since infection and calculi of the common duct are nearly always secondary to cholecystitis, the internist is urged not to delay in the transfer of such a patient to a surgeon. The internists who treat these patients first usually have the opportunity to see that surgery is instituted before liver and common duct damage occurs.

- Surgery should not be hasty nor should it be delayed unnecessarily. Before attempting surgery, the electrolyte balance should be re-established and in jaundice cases, vitamin K should be given in ample dosage.

- When a duct is opened, it should be carefully probed before inserting a drain and suturing the incision in the duct about it. Sulfanilamide powder (12 Gm.) should be scattered about the duct and in the abdominal wound.

- The failure of relief from symptoms following a cholecystectomy or a cholecdochostomy is usually indicative of a stone that was overlooked. Such pain is usually of organic rather than of functional origin.

- The nitrites (amyl-nitrate and nitro-glycerine) have a relaxing influence on the sphincter of Oddi and help facilitate the passage of a retained stone. Opiates, especially morphine, tend to increase the intra-ductal pressure.

- A case history of a patient, who following medication with nitrites, atropine and bile salts spontaneously passed two retained common duct calculi was cited.

- Gallbladder disease and cholelithiasis are rare among people of the colored race. Compared to the white race, the incidence

is one-twentieth as great. The occurrence of gallstones in many cases of sickle cell anemia was noted.

10. An analysis of 2,602 cases of biliary tract disease was presented. Biliary calculi were found in over 47.2 per cent of the 2,548 cases of cholecystitis among 250,065 hospital admissions during the past ten years at St. Vincent's Hospital and Harlem Hospital. Nine per cent of those who had stones, had their stones in the common duct, but only 5.5 per cent of the patients with gallbladder disease who were operated upon had stones recovered from their common ducts, and 6.6 per cent had their ducts opened and drained. Fifteen hundred seventy-five of the total cases were operated upon.

11. There is some similarity in incidence of common duct surgery and common duct stones in the 4,881 operative cases of cholecytic disease comprised of the series of 3,306 operative cases of gallbladder disease on the surgical service of Post-Graduate Hospital, in seventeen years reported by Heyd and Hotz<sup>13</sup> and the 1,575 cases of cholecytic disease on the surgical service of St. Vincent's and Harlem Hospitals in the past ten years. These figures differ greatly from the statistics of other authors who report a much higher incidence of common duct drainage and stones.

12. This low incidence of common duct stones probably may be attributed to the fact that the common ducts were opened and probed in such a small percentage of cases. Those patients seen in the follow-up clinics, who still complain of pain persisting in the right upper quadrant following cholecystectomy are possibly bearing pain from stones that were inadequately searched for, or from chronic infections of the common duct which were not recognized.

13. Surgery of the gallbladder and bile ducts without becoming audacious should, it would seem, become less conservative but more thorough and radical. The percentage incidence of common duct stones varies in proportion to the number of common ducts which are drained. An

analysis of over 9,272 operative cases of cholecystitis reported in the literature bears proof of this assertion.

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DIFFUSE hypertrophy (of the female breast) is of a progressive nature, the growth being either rapid or slow, and with little or no tendency to spontaneous cure. In cases of virginal hypertrophy, arrest of this condition is rare.

# MORTALITY RATE FROM ACUTE APPENDICITIS IN A MUNICIPAL HOSPITAL

LOUIS R. SLATTERY, M.D. AND

Assistant Visiting Surgeon, Bellevue Hospital

NEW YORK, NEW YORK

J. WILLIAM HINTON, M.D.

Visiting Surgeon, Bellevue Hospital

THE high incidence of death from appendicitis in the United States has made the management of this disorder of the greatest importance to all members of the medical profession. Especially is it of concern to surgeons, to whose care the majority of cases are usually consigned. In 1939, in the United States appendicitis stood fifteenth as the cause of death with 14,113 fatalities.

All factors concerned with the incidence, the onset and the treatment of this disorder are matters for pertinent investigation. In an attempt to throw further light on the morbidity and mortality factors concerned in this disease we have investigated carefully 677 cases of acute appendicitis and its complication in which the patients have been operated upon on the Fourth Surgical Division of Bellevue Hospital in New York City. This study covers the years 1928 to 1939 inclusive and includes only proved cases of acute appendicitis. All subacute, chronic, recurrent and mechanical disorders were eliminated.

The surgical approach will be discussed in some detail later. In general it consisted of immediate operation, adequate exposure, generally through rectus splitting incisions, protection of adjacent bowel from contamination and drainage of the abdomen when indicated.

**Mortality Rates.** From 1928 through 1939, 677 patients with acute appendicitis followed by various complications, have been operated upon on the Fourth Surgical Division at Bellevue Hospital. These cases have been subdivided into acute appendicitis, localized peritonitis, abscess and spreading or general peritonitis. As the differentiation at operation between local-

ized and spreading peritonitis is inaccurate at best, these two groups have also been considered as one. In none of these cases reported was sulfanilamide given intraperitoneally or orally. An analysis of the mortality in these cases is given in Table I.

TABLE I  
MORTALITY FROM APPENDECTOMIES, 1928 TO 1939

Diagnosis	No. Cases	No. Deaths	Deaths, Per Cent
Acute appendicitis.....	474	8	1.6
Local peritonitis.....	67	4	5.9
Abscess.....	88	7	7.9
General peritonitis.....	48	16	33.3
All peritonitis.....	115	20	17.3
Total.....	677	35	5.1

Further investigation of these cases revealed that there had been a surprising drop in the mortality of the cases during the latter half of this twelve-year period. This is evident from a glance at Table II in which comparison is made between the 1928 to 1933 and the 1934 to 1939 periods. It will be noted that the mortality rate dropped in the second period to nearly half of that in the earlier period (6.3 to 3.4 per cent). The greatest rate of decrease was in the acute cases but the decrease in the percentage of deaths was also very marked in the cases of general peritonitis.

Two important reports have recently appeared on the mortality rate in appendicitis. Reid and Montanus<sup>1</sup> gave data on 1,153 cases treated at the Cincinnati General Hospital from 1934 to 1938 inclusive. Haggard and Kirtley<sup>2</sup> summarized the reports on 2,777 cases treated from 1919 to

1935 in the hospitals of the University of Minnesota, the University of Michigan, the University of Iowa and Vanderbilt University. These reports together with the

mortality rate include 232 cases of chronic appendicitis with only one death. If this group is excluded from their total, it is found that they had fifty-five deaths in 921

TABLE II  
COMPARISON OF MORTALITY IN 1928 TO 1933 PERIOD WITH THAT IN 1934 TO 1939 PERIOD

Diagnosis	1928 to 1933			1934 to 1939		
	No. Cases	No. Deaths	Deaths, Per Cent	No. Cases	No. Deaths	Deaths, Per Cent
Acute appendicitis	266	7	2.6	208	1	0.47
Local peritonitis	33	2	6.06	34	2	5.8
Abscess	60	6	8.6	19	1	5.2
General peritonitis	23	10	43.4	25	6	25.0
All peritonitis	56	12	21.5	59	8	13.5
Total	391	25	6.3	286	10	3.4

data from Bellevue Hospital are given for comparison in Table III.

A glance at these figures shows that the mortality rate at Bellevue Hospital compares most favorably with those obtained in the large teaching hospitals throughout the country, this is especially evident for the period 1934 to 1939, the average mortality rates being definitely lower for

TABLE III  
COMPARISON OF MORTALITY STATISTICS AS REPORTED FROM SEVERAL LARGE HOSPITALS

Diagnosis	Average Four Hospitals (Haggard and Kirtley), Per Cent	Cincin-nati General Hospital (Reid and Montanus) Per Cent	Bellevue Hospital		
			1928 to 1939, Per Cent	1928 to 1933, Per Cent	1934 to 1939, Per Cent
Acute appendicitis	0.49	1.03	1.6	2.6	0.47
Abscess	6.3	10.08	7.9	8.6	5.2
Local peritonitis	7.7		5.9	6.06	5.8
General peritonitis	41.2		33.3	43.4	25.0
All peritonitis		17.22	17.3	21.5	13.5
Chronic appendicitis		0.43			
Total	5.5	4.86	5.1	6.3	3.4

Bellevue. Moreover, Reid and Montanus, whose data cover approximately the same period (1934 to 1938) in computing their

cases, or an average mortality rate of 5.97 per cent.

*Effect of Mortality Rate of Experience of the Operator.* Haggard and Kirtley quote Bowers to the effect that "The mortality from appendicitis decreases with the experience of the surgeon." Detailed investigation into the experience of the operators attending these 677 cases at Bellevue presents no data to warrant any such assumption in these cases. No increased experience by members of the surgical staff was responsible for the decrease in mortality, for only two of these operations were performed by the full attending and very few by the associate attending surgeons.

On the contrary, the operations were performed in two-thirds of the cases by the house staff who had had at the most two years of surgical training. Indeed one-third of the house staff had had only eighteen months' training. These relatively inexperienced men numbering seventy-two, performed 410 of the 677 operations with a mortality of only 3.4 per cent. The remaining 267 cases with a mortality rate of 7.8 per cent were operated upon by twenty-eight members of the attending staff. Obvi-

ously, the attending staff operated upon the more seriously ill patients.

From these data it is evident that no increased surgical skill was responsible for the decrease in mortality.

*Sex and Age of Patients.* Our data show that appendicitis was more common among males than females. Of our 677 cases 465 were men and 212 women.

As is shown in Table IV, appendicitis is far more frequent in the second and third decades of life than in later years. In all, 208 cases were in the twelve to twenty-year group and 225 cases in the twenty to thirty

TABLE IV  
AGE OF PATIENTS BY DECADES

Diagnosis	12-20	20-30	30-40	40-50	50-60	60-70	Over 70
Acute appendicitis	163	171	81	40	16	3	1
Local peritonitis	17	22	8	11	5	0	3
Abscess	17	22	18	17	9	0	3
General peritonitis	11	10	6	10	5	5	0
Total	208	225	113	78	35	8	7

year group. The incidence of the disease became progressively less as the age increased. No children under twelve years are included in this material as these patients are cared for on the Children's Surgical Service.

*History of Previous Attacks.* In Table V are given data concerning the history of previous attacks of appendicitis.

TABLE V  
HISTORY OF PREVIOUS ATTACKS

Diagnosis	No. of Cases	Per Cent
Acute appendicitis	114	24.05
Local peritonitis	16	23.8
Abscess	12	13.6
General peritonitis	13	27.08

It appears from these figures that approximately one-fourth of the patients operated upon had suffered from previous attacks of the disease.

*Duration of Symptoms.* In order to determine whether the duration of symptoms played a rôle in the difference in

mortality rates between the two groups of cases an analysis was made of this factor. These data are presented in Table VI.

TABLE VI  
DURATION OF SYMPTOMS

Diagnosis	1928 to 1933	1934 to 1939
Acute appendicitis	39 hr.	29 hr.
Local peritonitis	54 hr.	48 hr.
Abscess	5.6 days	10.2 days
General peritonitis	52 hr.	56 hr.

From this table it is to be noted that there was a definite shortening of time between the development of the symptoms and operative intervention in the cases of acute appendicitis. Reid and Montanus report a similar decrease. It may possibly play a rôle in the decreased mortality of this group.

In the cases of abscess the duration of symptoms is nearly doubled in the later group, the duration of 10.2 days, on the average, as compared with 5.6 days in the earlier group. Haggard and Kirtley believe that abscesses operated upon during the third, fourth or fifth day, at the height of the attack, result in a very high death rate. This statement is apparently borne out by our figures, from which it may be seen that the death rate from abscess in the earlier six-year period with a duration of symptoms of 5.6 days was 8.6 per cent as compared with 5.2 per cent during the period in which the average duration of symptoms was 10.2 days. Reid and Montanus, who reported that in abscesses the elapsed time between symptoms and admission to the hospital was 129.6 hours for the 1915 to 1933 period and 145.9 hours for the 1934 to 1938 period, also had a slightly decreased mortality for the longer time—10.08 per cent for the later period as compared to 11.4 per cent for the earlier one.

No marked difference in the duration of symptoms was seen for either local or general cases of peritonitis. In the former instance the length of time during which

symptoms were present dropped from fifty-four to forty-eight hours. The mortality rate likewise dropped from 6.06 to 5.8 per cent. This difference is so small as to be immaterial. In the cases of general peritonitis the average duration of symptoms increased from fifty-two to fifty-six hours. The mortality, however, dropped from 43.4 to 25 per cent. It is evident that the decrease in mortality in the cases of peritonitis cannot be ascribed to any change in the length of time during which the symptoms were present before the patients presented themselves for treatment.

TABLE VII  
HISTORY OF ADMINISTRATION OF CATHARTICS

Diagnosis	One Cathartic	Two or More Cathartics	Enema	Cathartic and Enema	Total
Acute appendicitis . . .	95	23	28	23	169
Local peritonitis . . .	18	7	9	5	39
Abscess . . . . .	13	12	9	5	39
General peritonitis . . .	14	5	3	0	22
Fatalities . . . . .	7	5	4	1	17

*Catharsis.* Many papers have been written on the dangers of administering laxatives to patients suffering from appendicitis. Concerted efforts have been made from time to time to acquaint the public with the dangers of taking such medicaments for

scor. In our series, seven patients had taken cathartics on the order of the physician. Fortunately, none of these patients had fatal outcomes. Reid and Montanus reported that cathartics had been prescribed by physicians in twelve of their 1,153 cases.

The cathartic history of our cases is presented in Table VII.

In our entire series of 677 cases there were thirty-five fatalities. As may be seen from the above table, seventeen of these were associated with the administration of cathartics and enemas. Omitting from consideration the four cases in which enemas alone were given, thirteen fatalities were associated with cathartics. On the other hand, twenty-two patients died who had been given none. From these figures we are unable to draw any definite conclusions as to the rôle of cathartics in deaths from appendicitis.

*Operative Procedure.* Does the type of operative procedure have any effect on the mortality in cases of appendicitis? Incisions are always cited as a factor in mortality. There is a general concensus of opinion that the McBurney incision is associated with a much lower morbidity and mortality. The type of operative procedure used and the mortality ensuing have been analyzed for

TABLE VIII  
OPERATIVE PROCEDURE—1928 TO 1933

Diagnosis	Right Rectus Incision			Kam. Incision			McBurney Incision		
	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent
Acute appendicitis.....	246	7	2.8	11	0	0	9	0	0
Local peritonitis.....	32	2	6.2	0	0	0	1	0	0
Abscess.....	62	6	9.6	2	0	0	5	0	0
General peritonitis.....	21	10	47.6	1	0	0	1	0	0
All peritonitis.....	55	12	22.6	1	0	0	1	0	0

supposed attacks of "indigestion" which may, in reality, be attacks of appendicitis. Less generally admitted by the medical profession is the fact that physicians are themselves not free from criticism on this

our two series of cases in Tables VIII and IX. It will be seen that the mortality for the McBurney incision is lower than that from the rectus incision, but the number is so small that a fair comparison is impossible.

TABLE IX  
OPERATIVE PROCEDURE—1934 TO 1939

Diagnosis	Right Rectus Incision			Kam Incision			McBurney Incision		
	No Cases	Deaths	Per Cent	No. Cases	Deaths	Per Cent	No Cases	Deaths	Per Cent
Acute appendicitis	138	1	0.7	8	0	0	70	0	0
Local peritonitis	27	2	7.4	0	0	0	7	0	0
Abscess	13	1	7.6	0	0	0	5	0	0
General peritonitis	19	1	5.2	0	0	0	2	1	50
All peritonitis	46	3	6.08	0	0	0	9	1	11.1

It may, however, be of some significance in the decreased mortality found during the later period, that the number of McBurney incisions has increased and the

TABLE X  
TREATMENT OF APPENDICEAL ABSCESS (EIGHTY-EIGHT CASES)

Treatment	No Cases	Per Cent of Total	Deaths	Mortality Rate
Appendectomy (partial removal)	66 (4)	75 (6.2)	4 (0)	6.2 (0)
Drainage only	22	25	3	13.6

number of right rectus incisions has correspondingly decreased. This is especially evident in the cases of acute appendicitis. During the period, 1928 to 1933, 246 right rectus incisions were made for acute

appendicitis and only nine McBurney incisions. During the 1934 to 1939 period 138 right rectus incisions were made for acute appendicitis and seventy McBurney incisions. It must, however, be emphasized that during the later period the mortality from the right rectus dropped markedly—from 2.8 to 0.7 per cent. Greatly decreased mortality was also evident during the later period from the right rectus incision in cases of general peritonitis.

The type of incision is of added significance if we consider the mortality of general peritonitis operated upon under the mistaken diagnosis of perforated peptic ulcer. Here the mistaken diagnosis and the inappropriate incision prove to be a lethal factor, even if subsequently the McBurney incision is made. If doubt is present as to the presence of a perforated appendix, it certainly appears justifiable to uncover this

TABLE XI  
DRAINAGE AS PART OF OPERATIVE PROCEDURE

Diagnosis	1928 to 1933				1934 to 1939			
	Peritoneal Drainage		Mural Drainage		Peritoneal Drainage		Mural Drainage	
	No	Per Cent	No	Per Cent	No	Per Cent	No	Per Cent
Acute appendicitis	74	27.8	42	15.7	23	11.3	45	21.6
Local appendicitis	29	87.8	2	6.06	26	76.4	5	14.7
Abscess	68	98.8	0	0	19	100	0	0
General peritonitis	22	95.6	1	4.0	25	100	0	0

area first with a McBurney incision. The production and closure of such an incision, if done mistakenly, does not place the operator in the position of being unable to retrieve a difficult situation, such as is present when the abdomen has been invaded and explored through an upper right rectus incision.

The management of eighty-eight cases of appendiceal abscess is given in Table x.

From these figures it appears that somewhat better results were obtained when removal rather than drainage alone was undertaken.

The rôle played by drainage and particularly the type of drainage is also of interest in any discussion of the operative treatment of appendicitis and the treatment of its complications. The number of cases in which drainage was used and the type of drainage is given in detail in Table xi.

From these figures it appears that peritoneal drainage has been somewhat less popular during the later than during the earlier period investigated, and that mural drainage has become more generally used than formerly. We do not believe, however, that this difference in treatment has any material effect upon the mortality rate.

TABLE XII  
PREOPERATIVE COMPLICATIONS

Diagnosis	No. of Cases	Mortality
Small bowel obstruction by abscess.....	1	0
Pulmonary tuberculosis.....	4	0
Uncontrolled diabetic acidosis.....	2	1
Otis media bilateral.....	1	0
Cellulitis of scrotum.....	1	0
Gonococcal urethritis.....	1	0
Catheter lost in bladder before operation.....	2	0
Leuetic aortitis and hypertension.....	1	0
Asthma.....	1	0
Acute appendicitis in incarcerated hernia c. ileus.....	1	0

*Preoperative Complications.* Our series of cases were attended by a number of complicating factors which are listed in Table xii. This table needs no further

discussion. The number of cases in each classification is too small to allow conclusions to be drawn.

TABLE XIII  
POSTOPERATIVE COMPLICATIONS

Condition	No. Cases	Mortality	Comments
Pregnancy.....	5	1	3 aborted, 1 with fatal hemorrhage
Pelvic abscess.....	8	0	7 subsided, 1 drained spontaneously
Fecal fistula.....	10	0	4 closed at operation 6 closed spontaneously
Dehiscence.....	10	2	1 sutured, 9 packed
Ventral hernia.....	7		
Subphrenic.....	2	1	1 died, rupture into chest in recovery, drainage
Phlephlebitis.....	2	2	
Gas infection abdominal wall.....	2	1	
Pneumonia.....	15	0	
Wound infections.....	71		
Hematoma.....	6		
Postoperative hemorrhage			
Retained appendices, drainage.....	4	1	
Obstruction.....	7		
Embolus.....	2	0	
Abscess of abdominal wall.....	2	1	
Atelectasis.....	4	0	
Phlegmon of abdominal wall.....	1	1	
Delirium tremens.....	1	0	
Tonsillitis and pharyngitis.....	8	0	
Phlebitis.....	3	1	
Fall out of bed, 1 hour postoperatively.....	1	0	
Abscess of L O I H sac, abscess.....	1	0	
Perirectal abscess.....	1	0	
Cellulitis of hand.....	1	0	
Urethral stricture, dehiscence.....	1	1	
Epileptic convulsions.....	1	0	
Cystitis.....	1	0	
Bronchitis.....	1	0	
Acute rheumatic carditis.....	1	0	
Abscess of back.....	1	0	
Cardiac decompensation and fibril.....	1	0	

*Postoperative Complications.* The post-operative complications are listed in Table XIII. From this table it will be seen that wound infections were comparatively common, occurring in seventy-one of the 677 cases or in approximately 10 per cent. Aside from this complication the table speaks for itself. Only rarely was the post-operative complication associated with a fatal outcome.

*Causes of Death.* The causes of death are listed in Table XIV. The predominating cause of death was peritonitis; this accounts for twenty-seven of the thirty-five fatalities. Pneumonia was purposely omitted, as we believe it is of only secondary importance as a terminal manifestation. All fatal cases bear the inevitable note concerning the physical signs to be found in the lungs, and it is interesting to note that these can dominate the postoperative picture to such an extent that the mild abdominal distention present is ascribed to the pneumonia process. Autopsy quickly apprises us of the true situation. It seems safe to assume that control of the ileus in peritonitis by intubation has been a factor in reduction of mortality.

TABLE XIV  
CAUSES OF DEATH

Cause of Death	No. Cases
Generalized peritonitis.....	27
Embolism or aspiration during lavage.....	1
Pylephlebitis.....	2
Subphrenic abscess .....	1
Postoperative hemorrhage.....	1
Shock.....	1
Small bowel obstruction.....	1
Postabortal uterine hemorrhage.....	1

*Diagnosis and Its Difficulties.* The diagnosis of appendicitis is not always a simple matter. This was called emphatically to our attention by one of our cases at Bellevue. The patient was watched on the ward for a suspected appendicitis for four days. Operation was determined upon only when signs of peritonitis appeared. The outcome, unfortunately, was death.

It is well enough to warn the public of the danger of appendicitis, and to attempt to educate them to call their physician

promptly in attacks of abdominal pain. But what happens when they do call us? Have we clearly in mind the diagnostic criteria of the disease or will we, as was the case in the patient mentioned above, find ourselves unable to make a definite diagnosis until it is too late for successful operative intervention?

The classic textbook picture of the physical findings in acute appendicitis are not those of early appendicitis. Delay, waiting for spasm and rebound tenderness to appear, will result in a large percentage of cases of peritonitis. It is essential that we remember the mechanism of production of peritoneal pain and muscle spasm in appendicitis, and stress the fact that these are produced only when peritoneal involvement has begun.

Symptomatology may be an important factor in mortality statistics. It is apparent, on reviewing our case histories, that it was not pain that drove a patient to the hospital but the onset on nausea and vomiting. This is borne out especially in the cases of abscess and peritonitis. In many instances, these patients were able to go about their work and do everything they normally did. The only departure from normal was a mild ache in the right lower quadrant. This discomfort was not sufficient to drive the patient to a doctor. Immediately, however, when vomiting began and general discomfort became great, medical advice was sought.

A review of individual case histories plainly demonstrates that little diagnostic reliance could be placed on the patient's history, which in many instances is bizarre, to say the least, due to his etiological concept of the disease. In 15 per cent of the cases it was believed that the disorder started with a dietary indiscretion. In shifting the wheat from the chaff in the patient's history it is essential to remember that pain precedes nausea and vomiting, and to try to elicit the facts on these points out of the patient's vagueness. When there has been dietary indiscretion, nausea almost always precedes abdominal pain.

*Physical Signs.* Physical signs require careful evaluation to make an early diagnosis. It can be seen in Table xv that classic textbook physical signs of tenderness, spasm and rebound tenderness are present in only slightly more than 30 per cent of our cases. This means careful attention must be given to the patient with abdominal tenderness regardless of the lack

TABLE XV  
PHYSICAL SIGNS

Physical Signs	No Cases	Per Cent
Tenderness alone	152	22.4
Tenderness and rebound tenderness	107	15.7
Tenderness and rigidity	204	30.1
Tenderness, spasm, rebound tenderness	212	31.3
Palpable abdominal mass	58	8.5
Rectal tenderness	332	47.5
Negative rectal examination	162	23.9
Rectal not done	183	27.0

of corroborative inflammatory signs. Although these signs in general parallel the severity of the underlying process, it is worth noting that a spreading peritonitis may be present without abdominal signs other than tenderness. This situation was present in patients presenting themselves late in the disease with marked toxemia and dehydration.

Attention is called to the fact that a palpable mass is not necessarily a sign of abscess, it being present in twelve acute cases, six cases with local peritonitis and five with general peritonitis. A mass was actually palpable in only thirty-five of the eighty-eight appendiceal abscesses proved by operation, an incidence of 39.7 per cent.

Rectal tenderness as the table indicates was present in almost half of the cases. It is worth pointing out that in three of the cases of abscess the mass was palpable only by rectum.

*Diagnostic Value of Leucocyte Count.* The leucocyte count is properly held as only a minor diagnostic aid. This is borne out in our series of cases; the average results are presented in Table xvi. The

TABLE XVI  
LEUCOCYTE COUNT (AVERAGE)

Diagnosis	Leuco-cytes	Poly-morpho-nuclears, Per Cent	Normal, Per Cent
Acute appendicitis	14,400	84	14.8
Local peritonitis	16,200	86	9
Abseess	15,900	84	12.7
General peritonitis	15,300	85	23.4

average blood count was definitely increased in all classes of cases, but the amount of increase was not very great. Moreover, in a number of cases the blood count was normal, as shown in the last column of the table.

We believe that it is especially significant that of the sixteen patients who died of general peritonitis, six had normal leucocyte counts. We are also of the opinion that in such instances this laboratory test is of definite prognostic value.

*Diagnostic Value of Patient's Temperature.* As a diagnostic aid, the temperature is no surer criterion than the leucocyte count, as is evident from Table xvii. True the temperature in all classes of cases does show an increase, rather marked in the cases of general peritonitis. Unfortunately, however, from a diagnostic viewpoint, from

TABLE XVII  
AVERAGE ADMISSION TEMPERATURE

Diagnosis	Average Temperature, °F.	Normal, Per Cent
Acute appendicitis	100.8	15.5
Local peritonitis	100.9	10.6
Abseess	100.9	11.4
General peritonitis	101.3	15.5

10.6 to 15.5 per cent (depending on the type of case) had perfectly normal temperatures.

*Diagnostic Value of Pulse Rate.* From Table xviii it is evident that the pulse rate cannot be taken as a significant diagnostic factor in appendicitis. Indeed, in approxi-

TABLE XVIII  
AVERAGE PULSE RATE

Diagnosis	Pulse Rate	Below 90— Per Cent of Cases
Acute appendicitis	94	28.6
Local peritonitis	99	22.3
Abscess	98	19.3
General peritonitis	98	25.0

mately one-fourth of the cases the pulse was below ninety. The average pulse rate in all classes of cases was below 100.

*Question of Conservatism in Appendectomy.* The question has arisen during the past decade as to the advisability of conservative management in the late cases of appendicitis. Many authors report significant decreases in mortality with these measures. In reviewing our material it is difficult to formulate criteria for selection of these cases. The presence or absence of a mass has particularly been studied as a possible indicator of a localized process. It is important, however, to note that only 39.7 per cent of our appendiceal abscesses presented masses at the time of admission. The temperature likewise is not of help in the making of a decision to procrastinate. Many of our acute cases presented themselves with temperatures over 102°F., the underlying factor in these instances, apparently, being dehydration and acidosis. We, however, tend toward immediate operation with fluid administration by vein during the immediate preoperative and operative period. It is evident from our material that acute cases would have gone on to peritonitis had some of the so-called indications for conservative management been employed.

#### COMMENT

From our investigation of 677 cases of acute appendicitis and its complications as treated surgically at Bellevue Hospital, we have reached the conclusion that the lessened mortality which has been evident

in later years is due not to any improvement in surgical technic but to the better general management of these cases. We attribute the lowered mortality rate to the universal use of parental fluids, to the use of blood transfusions and to the excellent work performed by the Department of Anesthesia.

When this statistical review was started, it was our purpose to analyze all pertinent facts pertaining to acute appendicitis and its complications. There were no preconceived ideas as to the management of any phase of the disease and it is interesting when all the data have been analyzed that no one method of attacking this disease could be given credit for our favorable results.

#### CONCLUSIONS

1. It would seem that the mortality in this series should represent the mortality for acute appendicitis throughout the United States in view of the fact that the 677 operations were performed by 100 different surgeons, seventy-two of whom were members of the house staff, who performed two-thirds of the total.

2. Although sulfonamide compounds have lowered the mortality in acute appendicitis, it played no part in this series as the study was concluded before the drugs were used.

3. Surgical delay in cases of abscess seems indicated from this study, but the diagnosis of an abscess is most difficult. In the eighty-eight cases it was diagnosed preoperatively in 39.7 per cent.

4. Removal of the appendix or simple drainage in the cases of abscess is still debated. In this series of eighty-eight cases twenty-two were drained with a 13.6 per cent mortality and sixty-six had an appendectomy with a 6.2 per cent mortality.

5. Nausea and vomiting are more important symptoms than pain in causing the patient to seek medical aid.

6. Tenderness and rigidity was present in only 30.1 per cent of the 677 cases and rectal tenderness in 47.5 per cent.

7. The leucocyte count is of limited diagnostic aid, and 14.8 per cent of the acute cases, 9 per cent of local peritonitis, 12.7 per cent of abscesses, and 23.4 per cent of general peritonitis revealed a normal count.

8. The temperature may be misleading in acute appendicitis as in 10.6 to 15.5 per cent the different types of the disease revealed a normal reading.

9. The pulse in this series was below 90 in 25 per cent of the total cases.

10. To assume that the lowered mortality of acute appendicitis in any institution in recent years is attributable to any one factor is probably erroneous.

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THE term "gynecomastia" signifies the abnormal development of the male breast. True gynecomastia is a physiological phenomenon characterized by a non-painful and non-inflammatory growth which presents to the touch the characteristic lobulation of the female organ.

# NONSPECIFIC MESENTERIC LYMPHADENITIS

LIEUT. R. W. POSTLETHWAIT, M.D.,  
Chief of Surgical Service, Station Hospital  
FORT MYER, VIRGINIA

WILLIAM O. SELF, M.D.  
PALMERTON, PENNSYLVANIA

AND  
ROGER P. BATCHELOR, M.D.  
PALMERTON, PENNSYLVANIA

**D**ESPITE the increasing interest in mesenteric lymphadenitis, the majority of discussions of the differential diagnosis of abdominal pain, including medical teaching, textbooks and current literature, consider only briefly or neglect the subject entirely. The papers by McLaughlin and Davis and by Ochsner and Murray are noteworthy exceptions. Because of the frequency of mesenteric lymphadenitis, its questionable etiology, and the difficulty of differentiation from acute appendicitis, we believe the subject cannot be emphasized too often. In 1939, Foster stated "it is high time that a more definite understanding be reached between practicing physicians and investigators of the disease syndrome called mesenteric lymphadenitis." Our aim is to further this understanding. The forty-four cases analyzed in this paper were encountered in a small clinic, serving a community in which both the practicing physician and the laity are "appendix conscious."

Wilensky believes that mesenteric lymphadenitis is always secondary to another process in the body, usually infectious. It is important that this primary disease be discovered and remedied, as it is found frequently that only after removal of the primary focus will the pain cease. Otherwise, normal appendices will continue to be removed for "chronic appendicitis" and useless treatment continued for "post-appendectomy adhesions" when the true cause of the pain lies in the persistence of the enlarged nodes in the mesentery. It is obvious that until accurate differential methods can be described, operation must

be carried out to exclude acute appendicitis. The removal of an appendix in which no pathological disturbance is present, however, does not relieve the surgeon of his obligation to continue his studies later in an attempt to find the real cause of the process.

The following classification based on the clinical picture is suggested by Rosenberg: (1) chronic mesenteric lymphadenitis, (2) acute mesenteric lymphadenitis, (3) acute fulminating mesenteric lymphadenitis, and (4) acute suppurative mesenteric lymphadenitis. Accordingly, our forty-four cases may be divided as follows: chronic seventeen, acute twenty-five, and acute fulminating two. We have had no cases of the suppurative type, but these have been reported by Tuberville, Borchard, Foster, Etchegorry, Porumbaru, Huggins, Segar and Rosenak, Schwyzer, and Wilensky and Hahn.

**Occurrence.** There are few reliable statistics available on the frequency of this condition. Struthers in two years had twenty-four cases of mesenteric lymphadenitis (including those of tuberculous origin) with 187 cases of appendicitis in the same period. Gage states that 60 per cent of his cases of chronic appendicitis showed mesenteric lymphadenitis. We consider our own statistics unreliable until January 1, 1941, because, prior to that time, we did not inspect carefully the mesentery of the terminal ileum in all cases of nonperforating appendicitis. Murphy, in 1908, mentioned enlargement of the mesenteric nodes in chronic appendicitis, while Noesske, in 1924, urged inspection of the mesentery in

cases with abdominal pain but an essentially normal appendix. As noted in the accompanying table, there has been a sharp rise in the number of cases in the past six months, and it is suggested that a diagnosis of mesenteric lymphadenitis would be made much more frequently if it were carefully looked for.

In this series of forty-four cases, there are twenty-six (59 per cent) males and eighteen (41 per cent) females. In 771 cases collected from the literature in which the sex was stated, there were 344 (44.6 per cent) males and 427 (55.4 per cent) females. The majority of reported cases are young, usually below thirty, and this was borne out in this group. The distribution by decades was: one to ten years, fourteen cases (31.8 per cent); eleven to twenty years, nineteen cases (43.1 per cent); twenty-one to thirty years, ten cases (22.7 per cent); and one patient was age thirty-two years.

By some authors, seasonal variation is thought to be of importance. The distribution of our cases is noted in Figure 1. Since only the first six months of this year have been included, it is obviously not a true representation. The distribution of our cases has thus far been fairly even throughout the year. We have noted, however, an increase in cases after any change regardless of season which favors infections, either respiratory or gastrointestinal, such as a sudden cold rain in mild weather or the first warm period suitable for swimming. It is difficult to evaluate these factors, but the impressions gained were very definite.

**Etiology.** Both Wilensky and Ireland have contributed excellent summaries on the possible causes of mesenteric lymphadenitis. The suggested agents range from a foreign body (Küper) to a virus (White and Collins). Many, including Brown Lanson, Speese, Coleman, Short, Segar and Rosenak, Powers, Porumbaru, Luzuy, and Ybarz believe the appendix is the site of the initial lesion. Wilensky and Hahn, Pribram, Bell and others have called attention to the analogous anatomic ar-

rangements and relationships of the cervical lymph-nodes and lymphatic apparatus of the neck and the mesenteric lymph-

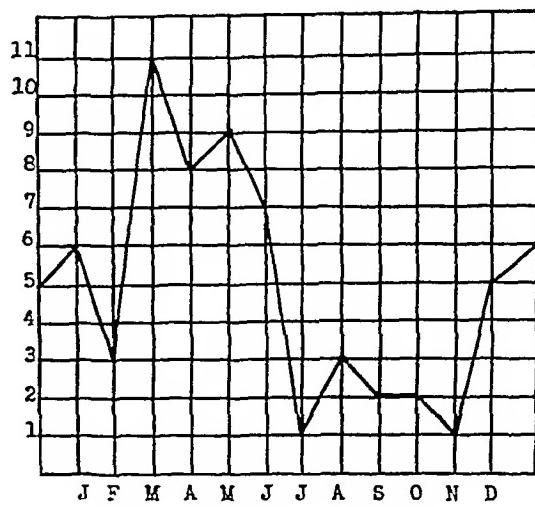


FIG. 1. Monthly rate of occurrence.

nodes and lymphatic apparatus of the intestine. Pribram has suggested that "the swallowing of lymphotropic bacteria from the tonsils may initiate inflammation of the appendiceal wall from where the mesenteric lymphatic system is then infected." It is doubtful if such an explanation is entirely or consistently true, but it serves as an excellent working basis, provided ileal wall be substituted for appendiceal wall in the statement. From the available evidence, it appears that the majority of cases are the result of the absorption from the lymphatic tissue of the ileum of bacteria, their toxins, or their decomposition products. The following case serves as an example:

W. H., a nineteen year old male, was first admitted because of a chronic draining sinus which followed a fracture of the left mandible. During the routine history, he mentioned that he had had frequent sore throats since the fracture occurred two months previously. Examination disclosed the tonsils to be enlarged and red. After satisfactory drainage of the osteomyelitis was established, he was discharged.

He returned two months later because of abdominal pain. The sore throats had continued, becoming more severe, and with each attack there had been abdominal pain. The present attack had started five days before;

the pain began and remained in the right lower quadrant, and was severe enough to confine him to bed. This, with the well localized tenderness, was considered sufficient to justify appendectomy. The appendix was grossly normal, but the lymph-nodes of the mesentery of the terminal ileum were enlarged and injected, the size varying from .1 to 1 cm. in diameter. The postoperative course was uneventful.

Following discharge, he continued to have exactly the same type of abdominal pain with recurrent tonsillitis. A month later the tonsils were removed. Streptococci, both hemolytic and nonhemolytic, were found in culture. Since the tonsillectomy, now a period of four months, abdominal pain has been completely relieved.

Further follow-up will be necessary, but it will only be by careful follow-up of all cases that the etiology of this symptom complex will be solved. A large group of cases, continuously observed, has not been reported.

**History.** Twelve of our patients had tonsillectomy and adenoidectomy from one to sixteen years prior to the onset of the disease. Seven patients gave histories of an acute upper respiratory infection shortly before or with the onset of the present illness. One patient, a fourteen-year old girl, had had slight leukorrhea since menarche two years before. Two patients gave a history of chronic otitis media, and the patient mentioned above had a chronic draining sinus from a low-grade osteomyelitis. Three patients described one similar attack of abdominal pain from one to two years before the attack requiring admission; three others had had several attacks during the year prior to the present illness; and four had been having recurring attacks for from two to six years. One patient had had an appendectomy six years before.

Twenty-six of the patients were seen within twenty-four hours of the onset of their illness and the remaining patients were seen within varying intervals up to two weeks. Pain was present in some stage of the disease in every patient; this was of varying intensity and location. In sixteen patients, the pain began and remained in

the right lower quadrant. In the remaining patients, the pain at onset was as follows: in two, right upper quadrant; in seven, across the entire lower abdomen; in five, epigastric; in five, perumbilical; and in nine, generalized. Of these twenty-eight patients, the pain later localized in the right lower quadrant in nineteen. Further classification of the pain revealed that in five the pain was slight; in fourteen, moderate; in twelve, severe; and the history does not record the intensity in thirteen. Six patients described the pain as being colicky in nature; five as cramp-like; ten as aching; and two as sharp. In three cases, anorexia was a prominent complaint. In nineteen patients, there was vomiting, varying from one to ten times. Five additional patients complained of nausea without vomiting. Six patients had taken laxatives without relief and five had received enemas without relief. Eight patients gave a history of diarrhea, consisting of from two to eight watery stools, in one of which blood was described. Only two patients complained of constipation.

The symptoms are presented in detail to emphasize the difficulty of differentiation from appendicitis and other acute abdominal conditions. Various minor points of contention occur throughout the literature in reference to the history. For example, White states that diarrhea is rarely present and constipation the rule, while we find the opposite to be true. Foster finds the pain more apt to be steady, continuous and dull. Freeman, in his early paper, noted the colicky paroxysms of pain which "come and go without apparent cause" and regarded this as a valuable diagnostic symptom. Speese, Coleman, and Bell have attached significance to this paroxysmal type of pain. This has also impressed us. We find that while in acute appendicitis the pain is usually progressively more severe and in the majority of cases constant, that of mesenteric lymphadenitis is almost always subject to frequent exacerbations and remissions. A case illustrating this follows:

C. K., a fourteen-year old white girl, was admitted because of severe right lower quadrant pain. For the year before, occasional attacks had occurred. For seven days before admission, there had been one to three attacks daily of severe right lower quadrant pain with nausea and vomiting. The day of admission, an attack had occurred in the morning, with extremely severe colicky pain and vomiting, which was followed by two watery stools. The attacks usually lasted several hours and she felt fairly well in the intervals. On examination she appeared moderately ill. The face was flushed. The temperature was 100°F. and the pulse rate was 96. The tonsils were enlarged and red. There was moderate tenderness in the right lower quadrant, no spasm, and with tenderness on the right by rectal examination. The urine was negative except for one plus acetone; the leukocyte count was 17,400.

At operation, the appendix was grossly normal. The lymph-nodes in the mesentery of the terminal ileum were enlarged, varying from 0.5 to 1.5 cm. in diameter. They were injected and the overlying peritonum appeared tense. The appendix was removed. Convalescence was uneventful.

The exact cause of the pain is problematic. Short believes it to be due to pulling on the mesentery during peristalsis. Speese and Rosenberg believe the cause to be the intestinal spasm. Brown feels the distention of the capsules of the nodes causes the pain. Freeman thinks it due to an irritation of the sympathetic filaments in the mesentery by the enlarged lymphatic nodes. We have found some correlation in the operative findings and the severity of the pain in that the greater pain is found in those cases which show a very tense peritoneum overlying the nodes, as if the node could be "popped out" with the slightest pressure. The patients with the chronic cases, however, when operated upon during an attack do not show this tenseness, but still have had the pain immediately before operation. For this reason, we cannot believe distention of the node capsule or overlying peritoneum can be the principal cause of the pain. It seems most probable that the pain is due to ileal spasm resulting

either from absorption of bacteria or their products, or from disturbance of the sympathetic fibers which pass through the nodes, or to both.

Foster, Marshall, and Wilensky have noted the frequency of tonsillitis and other respiratory tract infections in mesenteric lymphadenitis. This has also been our experience. Both McFadden and Worley frequently find nausea and vomiting in their cases. It has been our impression that this is seen less often in mesenteric lymphadenitis than in acute appendicitis. This, however, seems to be of less differential value.

*Examination.* The temperature was below 102°F. in thirty-six cases; in seven from 102° to 104°F.; and in one case was 104.4°F. The pulse rate paralleled the temperature elevation. One case showed slight icterus, interpreted as catarrhal in origin. (One of Brown's cases also showed jaundice.) Three cases showed acute follicular tonsillitis. In twenty-eight cases, there was definite evidence of infection in the upper respiratory tract. Perforation of the drums with slight purulent drainage was noted in two cases. In one patient, there was a draining sinus of the left mandible. In two cases, the spleen was enlarged, both extending about 4 cm. below the left costal margin. Acute epidermophytosis of the feet was noted in two cases. In eleven cases, the cervical lymph-nodes were enlarged; in two, the epitrochlear nodes were enlarged; in two, the axillary; in one, the femoral; and in one case there was generalized lymphadenopathy.

From the above, it can be seen that in approximately 77 per cent of our cases, a focus of infection was found at the time of the first examination. McKechnie and Priestley found a focus of infection in 60 per cent of their cases; Emmett in 44 per cent; Ingegno in 43 per cent; and Foster in 57 per cent. Foster, Pribram, Parini, and Brennemann call attention to the greater frequency of upper respiratory tract infection in mesenteric lymphadenitis than in acute appendicitis. We regard as particu-

larly important that in so many cases an infection is found which could logically act as the primary focus. It is highly suggestive that further search would reveal a primary focus in nearly 100 per cent of the cases of mesenteric lymphadenitis. We have not separated those cases with acute upper respiratory infections from those with no obvious primary focus, as suggested by Wilensky, as we believe they should all be included in one group. The fact that in some the source is easily demonstrable, while in others it is found with difficulty does not seem sufficient reason for the differentiation. The important point to be emphasized is that the causative agent is absorbed from the ileum, and that the source of this agent should be discovered.

Bell has also reported a case with palpable spleen. Careful hematologic and immunologic studies in our two cases failed to reveal any cause other than the primary infection which we believe also brought about the mesenteric lymphadenitis. Both were young white men, age twenty-one and twenty-two. Foster and McFadden have also noted enlarged nodes elsewhere frequently.

Examination of the abdomen showed tenderness in forty-two of the forty-four cases. In twenty-nine, this was in the right lower quadrant and varied in intensity. Graded on the basis of one to four plus: in five, the tenderness was one plus; in seven, two plus; in seven, three plus, and in ten, four plus. Tenderness was maximal in the epigastrium in one case, at the umbilicus in one, and generalized in three. There was tenderness across the entire lower abdomen in eight cases. In seven cases, there was increased muscle tone, and in four, there was rebound tenderness. Two patients showed slight abdominal distention and one was markedly distended. On rectal examination, twenty of the forty-four showed tenderness on the right. In the latter half of the series, an attempt was made to elicit the shifting tenderness as described by Klein. This consists in placing the patient on the left side for thirty

seconds or more, whereupon the tenderness, maximal in the right lower quadrant with the patient supine, shifts to the left lower quadrant. In only one of our cases of mesenteric lymphadenitis was this found. Curiously, two days after this patient was admitted, a twelve-year old white boy was seen with an acute upper respiratory infection, right lower quadrant pain, and tenderness which shifted with change in position. At operation, a gangrenous appendix was removed and no mesenteric lymphadenopathy noted. This is quoted merely to show that no definite pattern or sign occurs with dependable regularity in this condition.

We have noted with some frequency tenderness in the vicinity of McBurney's point extending to just above and to the left of the umbilicus. This is also mentioned by Gage, Ochsner and Murray, McFadden, and Schrager, and represents tenderness over the root of the mesentery. Freeman, McKechnie and Priestley, Ingegno, and Marshall have commented on the relative infrequency of spasm of the abdominal muscles, which has also been our experience. This is logical as the parietal peritoneum is rarely irritated in mesenteric lymphadenitis. Marshall and Foster have been able to palpate the enlarged mesenteric nodes in numerous cases. We have been unable to do this. McFadden describes an enlarged lateral sacral node on palpation by rectum. Mesenteric lymphadenitis is not to be confused with the acute iliac adenitis as described by Irwin.

In only twelve of our forty-four cases was mesenteric lymphadenitis made the primary diagnosis on admission. Thus in only 27 per cent of the cases was the original impression correct. Gross and Ladd state that mesenteric lymphadenitis is the most common disease which must be differentiated from appendicitis in children. As experience with mesenteric lymphadenitis increases, the diagnostic errors become less frequent. In this series, appendicitis was diagnosed twenty-one times, usually being called acute in type. Salpingitis and

enteritis were diagnosed two times each, and the following conditions once: pyelitis, Meckel's diverticulitis, pylorospasms, cystitis, uterine retroversion, spastic colon, tubo-ovarian abscess, and torsion of pedunculated ovarian cyst. From the list of errors given above, it is apparent that the statement of Klein: "the diagnosis of mesenteric adenitis is not an elusive mystery, but is rather simple" has not been true in our experience. The following case serves as an example of the difficulty encountered:

A. Z., a twenty-two year old white woman, was admitted because of abdominal pain. Her family, marital and past histories were irrelevant. Fourteen hours before admission, she was awakened by severe colicky, generalized, abdominal pain. The pain was most severe just below the umbilicus. She had vomited all liquids taken and an enema had afforded no relief. The temperature on admission was 99.4°F., the pulse rate 68, and respirations 18. The only positive finding on examination was moderate generalized abdominal tenderness, most marked midway between the symphysis pubis and umbilicus. The urine was negative and the leukocyte count 16,800.

She was watched for six hours. The pain became even more severe, the tenderness increased and board-like rigidity of the lower part of the abdomen developed. Rectal examination showed tenderness on both sides. Despite the essentially normal temperature and pulse rate, operation was thought necessary. Several possibilities were considered, with perforation of a Meckel's diverticulum thought the most likely. At operation, the findings were entirely negative except for typical, large, tense lymph-nodes in the mesentery of the terminal ileum. Recovery was uneventful.

*Accessory Clinical Data.* The leukocyte count showed wide degrees of variation. The lowest count was 4,200 and the highest 55,800. An average of the 44 counts gave 15,600. There were thirteen counts below 10,000; eighteen between 10,000-20,000; and thirteen over 20,000. Hemoglobin determinations and red blood cell counts were done on all patients and were not

unusual. Differential counts were recorded on twenty-eight patients. The majority showed a moderate polymorphonuclear leukocytosis; the highest being 93 per cent and the average 71 per cent. One case showed an eosinophilia of 10 per cent and in two other cases eosinophile counts of 4 per cent were noted. (One of Brown's cases had 6.5 per cent eosinophiles. Whether or not this tends to support the factor of allergy as an etiologic agent, as suggested by Ireland, is problematic.) Schilling hemograms showed a moderate tendency toward a shift to the left. Urine examinations were not unusual in all cases. Those who had vomited repeatedly had acetone, a few showed a trace of albumin, and a few white cells were found frequently on microscopic examination.

Oxyuris vermicularis were found by Ingegno in one case, by Ireland in one case, by Marshall in six, and by Heusser in several cases. In view of their findings, and because of occasional eosinophilia, from one to three stools were examined on twenty-four of our cases, and scrapings from the appendiceal mucosa were examined for parasites in ten others. All were negative and in no case were there signs or symptoms of this infection.

Sedimentation rates were done on twenty of the cases and varied from normal to 56 mm. per hour (Wintrobe). Kahn and Kline tests on eighteen of the patients were negative. From the work of Menefee and Poston, we realize that a single test does not rule out the possibility of Brucellosis. Nevertheless, macroscopic agglutination was carried out in twenty-four cases and all were negative. One of twenty-two patients subjected to intradermal test with 1:10,000 old tuberculin showed a positive reaction. In this single patient, a chest x-ray was negative and no calcified nodes found.

Heusser cultured colon bacilli in two of twenty-five cases. Adams and Olney found a hemolytic streptococcus in one node of two cultured. In culturing forty-eight nodes, Von Sassen obtained ten positives as follows: in five, *Bacillus coli*; in one, *coli*

and *Bacterium aerogenes*; in one, *coli* and hemolytic staphylococci; and in three, hemolytic staphylococci alone. Lawen, quoted by Von Sassen, found *Bacillus coli* in one case and hemolytic staphylococci in two others. Urech, in an unstated number of cases, cultured colon bacilli or enterococci from the nodes. Polichetti reports a diplococcus in a suppurative case. Goldberg and Nathanson cultured *Streptococcus hemolyticus* in one of eight cases. Gage has obtained an exceedingly high percentage of positive cultures. He reports finding an enterococcus in 93 per cent of sixty-five nodes cultured, either alone (67 per cent) or with the colon bacillus or a streptococcus. Marshall cultured *Bacillus coli* from nodes in two acute cases. Wilensky and Hahn found a Gram-negative bacillus in the abdominal fluid of one patient and recovered *Streptococcus hemolyticus* from the suppurative node of another. Lamson states that from the clinical course a streptococcus seems the most probable causative organism but offers no proof by culture. Kelly quoted an early case reported by Auguy in which *Bacillus coli* was cultured.

Lymph-nodes were removed and cultured aerobically and anaerobically in sixteen cases of this series. Positive cultures were obtained on two occasions. On the first, *Bacillus coli* was found. In the second case, the node selected for culture was a large one in the meso-appendix. A small Gram-negative diplococcus was found in both the aerobic and anaerobic cultures. This suggests two possibilities: Nodes near the appendix or bowel are more likely to yield positive cultures, and the appendix cannot be dismissed as the portal of entry, regardless of the anatomic evidence offered by Wilensky and by Klein.

The nodes of the mesentery are divided into three groups by Poirier and Cuneo: A primary group on the course of the terminal arterioles near the bowel, a second group at the level of the first anastomotic arch of the primary branches of the superior mesenteric artery, and a third group about

the trunk of the superior mesenteric artery. The filtering action of lymph-nodes is well known, and it may be that the selection of a node in the primary group in preference to one in the second group will mean the difference between a positive and a negative culture.

*Findings at Operation.* The operative findings in this series were quite similar to those described in other communications. All patients were operated upon and the diagnosis of mesenteric lymphadenitis either confirmed or discovered. In six of the patients a slight excess of clear fluid was found on opening the peritoneum. In one case, slightly blood-tinged fluid was found and in one other, there was a large amount of grayish watery material present. The appendix was described as being grossly normal or at most slightly hyperemic in thirty-seven of the forty-four cases. In one case, the appendix had been removed previously. The remaining six cases showed acute inflammation of the appendix, two of which were frankly gangrenous. The terminal ileum and cecum felt and appeared normal in all cases except one. There was no evidence of lymphedema in the mesentery or bowel. The lymph-nodes in the mesentery of the terminal ileum were enlarged to a varying degree. In every case, it was noted that there was progressive enlargement of the nodes from the border of the intestine toward the root of the mesentery. Usually, at the mesenteric border the nodes were from 1 to 5 mm. in diameter, gradually increasing in size centrally to more than 2 cm. in size at the mesenteric root. The appearance of the nodes and the overlying peritoneum also varied and could not in all cases be correlated with the clinical findings. In the more acute cases the nodes appeared extremely tense and hyperemic, the peritoneum seemed stretched over them. In the subacute and chronic cases, the reaction appeared to be subsiding and the nodes presented a dull, purplish-red hue with no peritoneal reaction. Nodes were removed for culture and section in sixteen cases. This procedure was without

difficulty and in no case was the circulation of the bowel endangered. The appendix was removed in forty-three cases.

Ireland found mesenteric lymphadenitis in a patient who had had appendectomy nine months previously. Schnitzler reports a similar case with appendectomy eight years before. In Foster's series, four had prior appendectomies. In our case, the patient had had appendectomy six years before her admission here. She gave a history of recurrent attacks of abdominal pain over a period of two years. Operation was done to suspend a markedly retroverted uterus and mesenteric lymphadenitis found.

In three of our cases, calcified nodes were found in addition to the acutely involved nodes. In one of these, an abdominal x-ray was made seven months after operation and there was no evidence of calcification. He had experienced no further abdominal distress. The exact interpretation of this is difficult. The two others have been seen more than a year after operation and they, too, have had no more pain. Brown had one case with definite calcified nodes at operation; x-ray examination eight years later showed a faint vague shadow of questionable calcification. Kirkpatrick reports a case of intestinal obstruction caused by calcified mesenteric nodes. Short and McFadden, Colt and Clark discuss the severe pain which is frequently caused by calcified nodes. Auchincloss states calcified nodes may cause symptoms by forming adhesions or bands, by other nodes lesions of like nature, but active and not scarred or calcified, and by the presence of the nodes alone. Scheckter studied calcified nodes found on routine x-ray examinations in relation to clinical symptoms and concluded that they did not cause pain and tenderness as often as is commonly thought.

Wilensky states that the lymphatic drainage of the appendix is such that only a congenital abnormality will produce a mesenteric lymphadenitis secondary to acute appendicitis. Six of our patients had definite acute appendicitis, both grossly

and on microscopic study. Two of these were gangrenous. Coleman reports that fourteen of his sixty-two cases, and Foster thirteen of his one hundred and fifteen cases had acute appendicitis and acute mesenteric lymphadenitis. Thus in 221 cases, 14.9 per cent had acute appendicitis, an incidence which seems considerably in excess of congenital abnormalities.

The acute fulminating type of mesenteric lymphadenitis is less frequently seen and the following case is one of the two which we placed in this classification:

K. R., a seven-year old white girl, was admitted because of severe abdominal pain. Her past history was negative except for a very severe upper respiratory infection one month before. For a week before admission, she had had a cold with moderate sore throat. Six hours previously, there had been the onset of extremely severe, colicky, abdominal pain, more marked in the lower part of the abdomen. There had been no nausea or vomiting, but anorexia was present. Her bowels were regular and no laxative had been administered. On examination, temperature was 102°F., pulse 130, and respirations 28. She appeared acutely ill, with flushing of the face and glassy eyes. The tonsils were markedly enlarged and red. The nasal mucosa was injected and there was a purulent nasal discharge. The heart and lungs were normal. The abdomen was moderately distended, with tenderness throughout, more marked in the lower part, and on the left greater than the right. There was spasm in both lower quadrants, which was marked, and also rebound tenderness. The femoral lymph-nodes were enlarged. On rectal examination, tenderness was present on the right. The urine was negative. The leukocyte count was 21,300 with 85 per cent polymorphonuclear forms.

On opening the peritoneum, there was an excess of slightly cloudy, sticky fluid. On smear, a Gram-positive coccus in clumps was found (later identified as *Staphylococcus aureus*). The entire peritoneum, with the appendix, cecum, and terminal ileum appeared hyperemic. The lymph-nodes in the mesentery of the terminal ileum were enlarged, firm and tense. The appendix was removed; no node was taken because of the positive smear. The abdomen was closed without drainage. Her postoperative course was uneventful. She

was given sulfathiazole 0.5 Gm. every four hours for forty-eight hours, and her temperature was normal on the third day after operation.

Wilensky has emphasized that "normals of size of lymph nodes have not been established and so fundamental diagnostic errors may occur." Mead concludes "visual differentiation is accurate, for the apparent size of a node is fairly indicative of its weight." We believe that in any case in which there are found a large number of lymph-nodes in the mesentery of the terminal ileum, measuring by estimation 0.5 cm. or more in diameter, pathologic enlargement may be assumed.

**Pathology.** Thirty-seven of the appendices removed showed no essential pathologic change. The remaining six presented the usual findings of acute appendicitis, with marked edema, polymorphonuclear leukocyte infiltration and areas of necrosis. The nodes removed showed only lymphoid hyperplasia with varying degrees of edema. There was no tubercle formation found.

**Postoperative Course.** In about 75 per cent of the patients, convalescence was uneventful following operation. The remaining patients had unusually trying courses; the main difficulties were abdominal distention and cramps which were extremely severe. Surprisingly, the degree of postoperative reaction could not be correlated with the severity of the illness before operation or the operative findings. Several of the patients with severe preoperative pain had little difficulty during convalescence, while two patients with chronic cases operated upon after the acute attack had subsided, had marked distress afterward. Further, most of the patients with cramps and distention responded well to the usual measures of clear liquid diet, hot packs, enema, and prostigmin, while a few were refractive to all therapy.

Usually, the temperature was normal by the third day, the patient out of bed on the fifth and home on the seventh. In two cases, there was an exacerbation of their upper respiratory infection. Five cases received

one of the sulfonamides with perhaps some beneficial effect.

TABLE I  
RATE OF OCCURRENCE AT THE PALMERTON HOSPITAL

Year	Appendectomies*				Mesenteric Lymphadenitis	Per Cent
	Acute	Recurrent	Incidental	Total		
1939....	96	42	45	183	3	1.6
1940....	90	44	43	177	20	10.1
First 6 mos. of 1941...	43	17	25	85	35	29.1

\* Total appendectomies for period indicated; acute refers to appendectomy for acute suppurative, gangrenous, or perforated appendicitis; recurrent includes "chronic," subsiding, or interval cases; incidental appendectomies were done at other operations, usually gynecologic. This chart includes fourteen additional cases not included in the analysis of symptoms, etc.

No serious postoperative complications occurred in this series. Pribram had one death in which autopsy showed mesenteric lymphadenitis. Sobel and Stetten report one death of bronchopneumonia three days postoperatively. Adams and Olney had a patient who died five and one-half hours after operation; no definite cause was found. Ireland in twenty-two cases had one death due to peritonitis from rupture of a suppurative node (*Streptococcus hemolyticus*). McKechnie and Priestly also had one death in their series. Coleman reports that one of his patients, who had acute appendicitis and acute mesenteric lymphadenitis combined, developed peritonitis with paralytic ileus and expired. We have found no report of postmortem examination of the mucosa of the terminal ileum.

**Follow-up.** As indicated in Table II, of 371 reported cases followed, the various authors report cures in 67.9 per cent. These cures were after appendectomy and general hygienic measures. Marshall had cure of symptoms with improved general health "in a large proportion but admittedly not all" of his cases.

We have been able to recall and examine twenty of our forty-four cases after inter-

vals of from four to twenty-four months. Seventeen patients were completely well. Two patients had had gastrointestinal disturbances which were in no way similar to the symptoms preceding operation. One patient, a six-year old boy, was particularly interesting. He had continued to have pain in the right lower quadrant with each upper respiratory infection. Examination showed the tonsils to be markedly enlarged and chronically infected. Tonsillectomy was advised but has not as yet been carried out.

TABLE II  
RESULTS OF FOLLOW-UP AFTER APPENDECTOMY

Author	No. of Cases Followed	Completely Well
Brown	30	30
Rosenberg	29	10
Adams and Olney	11	11
Sobel and Stetten	20	9
Gage	22	14
Wise	8	6
Klein	50	0
Ireland	20	16
Coleman	62	62
McKechnie and Pricstley	49	36
Ingegno	30	25
Strombeck	40	33
	371	252

#### SUMMARY

Nonspecific mesenteric lymphadenitis is a symptom complex which occurs much more frequently than is generally acknowledged. This assumes that the mesentery of the terminal ileum is inspected in all suspicious cases. The symptoms are found usually in children and young adults. Despite the statements of others, upper respiratory infections occur much more frequently in mesenteric lymphadenitis than in appendicitis. The etiology remains to be proved, but it appears to be secondary to infection elsewhere in the body, usually the gastrointestinal or respiratory tracts.

The factors most useful in differential diagnosis are the colicky recurring nature of the pain and the distribution of the

tenderness over the root of the mesentery. The laboratory findings are of little aid. The leukocyte count varies markedly and cannot be correlated with the clinical findings. We cannot agree with those who consider that appendectomy alone cures the majority of these patients. We do agree, however, that operation is indicated because of the inability to exclude acute appendicitis in most cases.

#### CONCLUSIONS

1. Mesenteric lymphadenitis is a symptom complex of frequent occurrence which has not received due emphasis in texts and papers considering the causes of abdominal pain.
2. The node enlargement is always secondary, and in most cases, the primary source can be found and eradicated.
3. Operation with appendectomy is the treatment of choice unless more vigorous differentiation can be made.
4. Careful study and follow-up will lend much to the solution of the etiology, accurate diagnosis and proper treatment.

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ANY operation on the breast which subjects the patient to radial or longitudinal incisions predisposes to more or less scarring. This should be avoided. Scars are constantly reminding the patient of the operation which she has undergone and, should there be a tendency to keloid formation, matters are much worse because of the effects produced by the keloid.

# DIFFERENTIAL DIAGNOSIS AND TREATMENT OF ACUTE ABDOMINAL INJURIES\*

METHOD EMPLOYED AT THE UNIVERSITY OF MINNESOTA HOSPITALS

CHARLES E. REA, M.D.

ST. PAUL, MINNESOTA

WITH the increasing number of automobile accidents in peace time and the frequency of bullet wounds to the abdomen in time of war, the problem of abdominal injuries becomes one of paramount importance. Most writers on this subject are concerned with the treatment and end results. However, both treatment and end result would be better if a more accurate diagnosis of the type of abdominal injury could be made.

In 1935, Wangensteen reviewed the general problem of abdominal injuries. He concluded that in all acute abdominal injuries, two factors influence the type of treatment to be given: First, whether the trauma was blunt or penetrating, and second, whether a hollow or solid organ was injured. It may be said that (1) nearly all injuries caused by penetrating trauma and certainly all injuries perforating hollow viscera should be operated upon as soon as the condition of the patient permits. (2) Injuries due to blunt trauma may or may not be operated upon, depending upon whether a hollow or solid viscous was injured. Subcutaneous injuries of the abdominal organs occur in the following order of frequency: Liver, spleen, kidney, intestine, stomach, bladder and pancreas (Greil). (3) Injuries to solid viscera such as liver, spleen or kidney are preferably treated conservatively as long as the blood pressure and pulse are stabilized and there is no marked fall in the hemoglobin and erythrocyte count.

Thus, the whole problem of the treatment of acute abdominal injuries resolves around this question: Given a history of trauma to the abdomen, how can one be

certain whether a hollow or solid viscous has been injured? The purpose of this paper is to give a method of differential diagnosis of acute abdominal injuries employed on the Surgical Service of the University of Minnesota Hospitals, which has proved of distinct value.

## ABDOMINAL INJURIES CAUSED BY BLUNT TRAUMA

In early cases of abdominal injury, the temperature, pulse, respiration, blood pressure, leucocyte count or degree of shock rarely give any information of value as to the location or degree of injury to the abdominal organs. The best indication of what organ has been injured is the location of the trauma.

Injuries to the omentum, mesentery and pancreas are impossible to diagnose with any degree of certainty. Fortunately, they do not occur very often. In reality, it is injury to the solid organs such as the liver, spleen and kidney and to the hollow viscera such as stomach, large and small intestine and bladder that is of diagnostic importance in abdominal injuries.

1. *Liver.* Injury to the liver may be suspected by the location of the trauma, the presence of liver tissue protruding from the wound, tenderness or abnormal dullness or percussion over the normal course of the ascending colon and elevation of the right diaphragm.

2. *Spleen.* When the spleen has been ruptured there is tenderness and abnormal dullness on percussion in the left upper quadrant; the dome of the left diaphragm may be elevated or there may be signs of a left pleural effusion. The hematoma may be

\* From the Department of Surgery, University of Minnesota Medical School.

felt on bimanual palpation. The ribs of the lower left chest are often fractures.

3. *Kidney.* Hematuria, pain in the back, a mass (hematoma) palpable in the flank should make one suspect renal injury. An x-ray of kidney, ureter and bladder and intravenous pyelogram may be diagnostic.

4. *Bladder.* In suspected rupture of the bladder the location of the trauma is helpful. As mentioned before, about half of these cases are associated with fractures of the pelvis. The patient will complain of hematuria, dysuria and oliguria or anuria. Failure to recover sterile saline injected into the bladder by catheter is not to be relied upon too strongly as a diagnostic sign of ruptured bladder. An important diagnostic measure is the cystogram taken not only in the anteroposterior and lateral views but also in the two oblique views. In making a cystogram it is better to inject a radiopaque substance, such as sodium iodide or diodrast rather than air (hoping to visualize the latter under the diaphragm by x-ray), as the chance of getting a negative result in rupture of the bladder is less when an opaque medium is used.

5. *Stomach and Large Bowel.* In injuries to the stomach and large bowel, where the viscera has been perforated, gas may be visualized under the diaphragm, especially on the right side. The history and location of the injury (compressed air forced into the rectum, impalement, foreign body in the rectum, etc.) will aid in the diagnosis of injury to the large bowel.

6. *Small Bowel.* When the small intestine has been rent by blunt trauma applied to the abdomen, the places that are the most likely to be involved are the two fixed portions: (a) near the ligament of Treitz and (b) near the ileocecal region. When the lower reaches of the small bowel are ruptured, gas is usually not visualized under the diaphragm by x-ray, due to the fine and intimate mixture of the gas with the food. In rupture of the retroperitoneal portion of the duodenum, the diagnosis may be made by the presence of gas around the kidneys by the roentgenogram. The diag-

nosis of rupture of the small bowel due to blunt trauma to the abdominal wall is the most difficult of visceral injuries to diagnose. Also it is surprising how indirect and relatively mild the trauma may be that causes rupture of the small intestine. One patient seen at this hospital had a tear in the terminal ileum after falling into a post hole and landing on her buttocks.

#### MANAGEMENT OF ACUTE ABDOMINAL INJURIES DUE TO BLUNT TRAUMA

When a patient who has suffered an acute abdominal injury due to blunt trauma is admitted in shock, it is imperative that the patient be brought out of shock before any diagnostic or therapeutic measures be directed to the abdominal injuries.

It is also a good rule to consider all patients in shock as though they had a head injury, fractured spine and abdominal injuries and *treat as such* until these possible injuries have been ruled out.

The diagnosis and treatment of patients with acute abdominal injuries due to blunt trauma are always easier if the patient is first seen two or three days after the injury than if they are seen immediately. As mentioned before, it is a tear in the small bowel that is most difficult to diagnose. Given a patient who has suffered blunt trauma to the abdomen, is not in shock and who on physical examination has pain, rigidity and tenderness of the abdomen, the diagnosis of injuries to the solid viscera will have to be made chiefly by the history, location of the trauma and the clinical signs discussed above. If a ruptured kidney is suspected, an x-ray of kidney, ureter and bladder and intravenous pyelogram are in order. If rupture of a solid organ is ruled out, an upright film of the abdomen should be made. If the roentgenogram fails to show free gas under the diaphragm, an open perforation in the stomach or colon is ruled out. If the rigidity, tenderness and even rebound tenderness are chiefly in the lower abdomen, a cystogram should be made to rule out a rupture of the bladder. If the cystogram is

negative, the patient should be explored, as there may be a tear in the small gut.

Some may say that a patient with an abdominal injury due to blunt trauma who shows signs of pain, tenderness and rigidity in the abdomen had best be operated upon. However, many patients with ruptured spleen, kidney and liver will be operated upon in such instances and it is known that most of these cases do well if not better under conservative therapy. The presence of gas under the diaphragm or extravasation of contrast media out of the bladder directs the surgeon's attention to the source of the peritoneal irritation. The upright film of the abdomen and cystogram are the best available methods of ruling out other lesions when considering perforation of the small gut. Unless procedures like peritoneoscopy come into more general use and give more accurate results, it is the only way that a differential diagnosis of a rupture of the small bowel can be made.

#### MANAGEMENT OF ACUTE ABDOMINAL INJURIES DUE TO PENETRATING TRAUMA

The introduction of the use of laparotomy for penetrating wounds of the abdomen, especially bullet wounds, was definitely an American contribution to surgery, although the first recovery from such an operation was reported by Kocher. In the period before the discovery of anesthetics and antiseptic methods, most surgical procedures were not only inadequate but were also doomed to failure because of subsequent shock and infection. Some surgeons, especially those with military experience, recognized that the ideal treatment consisted in opening the abdomen and repairing the injury. Many of the earlier surgeons, including Larrey, enlarged wounds due to firearms and repaired the damaged tissues, although they did not perform laparotomy in the modern sense.

A new era began with the advent of antiseptic surgery. Sims, in 1882, stated that laparotomy for bullet wounds was as

feasible as that for ovariotomy. The end results of such laparotomies were and are far from comparable, however. Oberhelman and LeCount, in a review of the literature from 1893 to 1918 reported that of 1,494 patients with bullet wounds treated by laparotomy, 52.8 per cent died. Even up to World War I, there was some question as to whether a policy of non-interference, surgical interference in every case, or interference under certain conditions should be employed in the treatment of gunshot wounds. Amat enumerates twenty different meetings of the French society of surgery in Paris from 1886 to 1891 at which this subject was debated. At the meeting of the American Surgical Association in 1887, the members were asked to express their opinions as to whether laparotomy should be performed for penetrating gunshot wounds of the abdomen involving viscera.

The most convincing report on the value of an immediate operative attack as contrasted to conservative treatment of gunshot wounds of the abdomen is that of Enderlen and Sauerbruch. In 1915, they treated fifty-two cases of gunshot wounds to the abdomen conservatively and forty-six patients, or 94 per cent died. Of 211 patients with intestinal injury treated by laparotomy ninety-two, or 44 per cent, recovered. This improvement in the survival rate even under the adverse surgical conditions of war certainly proves the value of surgical treatment of gunshot wounds of the abdomen. In peace time a similar result was observed by Oberhelman and LeCount. Between the years 1911 and 1924 at Cook County Hospital, Chicago, there were 343 instances of bullet wounds to the abdomen. Of these 301 had laparotomies, of which 185 died (61.4 per cent). Of forty-two patients not operated upon, thirty-seven or 88 per cent died. It should be stated, however, that most of the patients in the latter group were in poor condition upon entrance into the hospital and died subsequently of shock. These authors also found that in wounds of single viscera the organs liable to be injured were as follows: Small intes-

tine, liver, colon and stomach. The mortality of injuries to the small bowel was 48.7 per cent. When there were injuries of two or more viscera due to bullet wounds, the mortality was 80.7 per cent, compared to that of 34.2 per cent for those with injury to a single viscus. They believed that the most important single element aiding the recovery of the patients with bullet wounds of the abdomen is a short interval between the injury and the operation. Also the experience of the surgeon in dealing with this type of injury is important. It is noteworthy that, in Oberhelman and LeCount's study, bullets entering the sides of the abdomen cause the most deaths; those entering the front are more often fatal than those entering the back.

#### TREATMENT OF ABDOMINAL INJURIES DUE TO PENETRATING TRAUMA

It is generally accepted that patients who die of bullet wounds to the abdomen within the first twenty-four hours after injury die from shock; when death occurs after twenty-four hours, it is usually due to peritonitis.

It is imperative that the patient with penetrating wounds of the abdomen be operated upon as soon as possible, but if the patient is in shock, he should be given blood transfusions or plasma until he is out of the shock level. Also, all patients with penetrating abdominal wounds, whether in shock or not, are potential candidates for shock and should be given blood transfusions during the operation as a safety measure. In our experience the type or length of anesthesia are not so important if the patient is given a transfusion during operation. Blood transfusions should be considered as much a part of the surgical procedure as the abdominal incision and the closing of the perforation.

In most instances it is enough just to close any perforation of the gut. Oberhelman and LeCount found that in only a few patients do the wounds require section of the viscera or parts of the viscera.

Postoperative drainage is a matter of opinion and depends somewhat upon the amount of peritoneal contamination at the time of operation. There are no convincing studies to prove that drainage has any advantage over tight closure of the abdomen in gunshot wounds. More important is the use of suction applied to an indwelling Wangensteen or Miller-Abbott tube to keep the bowel (a) empty, to prevent paralytic ileus and (b) quiet to allow localization of any peritoneal exudate.

Recently there is evidence to show that sulfanilamide is of value in preventing peritonitis in experimental animals (Jensen, Varco, Rea). Clinically, it is impossible to judge its value as yet (Ravdin). Experimentally, however, it has more protective value when used before peritonitis has developed than when peritonitis is already present. At present, sulfanilamide in doses of 3 Gm. is powdered into the peritoneal cavity at the end of operation where there has been gross or suspected contamination, and postoperatively the drug is given by mouth, 60 to 90 gr. a day, or subcutaneously in doses of 125 cc. of an 0.8 per cent solution every four hours. The blood level of the drugs as well as the hemoglobin, erythrocyte and leucocyte counts are checked daily and the dosage regulated accordingly. It should be mentioned also that there is an impression at the Clinic of the University of Minnesota Hospitals that sodium ricinoleate 1 per cent in doses of 3 to 4 ounces, poured into the peritoneal cavity is of value in preventing peritonitis, but experimentally it is not as effective in the pre-peritonitis stage as sulfanilamide (Rea).

Postoperatively, the two complications to fear after gunshot wounds of the abdomen are peritonitis and pneumonia. Whether the former develops depends very much upon the factors present at and before operation, as the length of time before surgery, type and number of wounds, organ involved, etc. However, the resistance of the patient may be bolstered by means of continued siphonage drainage to

an indwelling intestinal catheter, blood transfusions, judicious administration of para-oral fluids, sulfanilamide, etc. Pneumonia may be prevented to a large measure by intratracheal aspiration of bronchial secretions after operation and subsequently as often as may be necessary, by encouraging the patients to cough, breathe deeply and to change their position frequently. The use of chemotherapy, especially sulfathiazole and antisera, is invaluable if pneumonia develops.

#### SUMMARY

In all acute abdominal injuries, two factors influence the surgeon in his choice of a surgical or conservative way of treatment: (1) Whether the trauma was blunt or penetrating and (2) whether a solid or hollow organ was injured. It may be said that nearly all penetrating wounds and certainly all perforations of hollow viscera should be operated upon as soon as the condition of the patient permits. The question, however, is: Given a history of either blunt or penetrating trauma to the abdomen, how can one be sure as whether a hollow or solid organ has been injured? The history, location of the trauma and clinical findings are of prime importance, but patients who complain of abdominal pain, rigidity and tenderness should have an upright film taken of the abdomen to rule out the presence of free intraperitoneal gas. If no free gas is seen, an open perforation of the stomach and colon is ruled out.

If the pain is in the lower quadrant of the abdomen, a cystogram should be made to rule out a tear in the bladder. If the cystogram and upright film of the abdomen are negative, and if the possibility of rupture of the liver, spleen and kidney are ruled out, the patient should be explored to rule out the possibility of a tear in the small bowel.

Injuries to solid viscera are best treated conservatively as long as the patient shows no signs of shock. While the mortality of penetrating wounds to the abdomen is about 50 per cent, the results following surgical treatment are far superior to those following non-interference.

The plan of pre- and postoperative care of such patients at the University of Minnesota Hospitals has been briefly outlined.

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# A ROENTGENOGRAPHIC AID TO THE DIAGNOSIS OF LEFT SUBPHRENIC DISEASE

MILTON G. WASCH, M.D.

Attending Radiologist, Jewish and Israel  
Zion Hospitals

AND

BERNARD S. EPSTEIN, M.D.

Assistant Radiologist, Jewish Hospital

BROOKLYN, NEW YORK

THE diagnosis of left subphrenic disturbances has long perplexed the radiologist. Until quite recently it could be suggested only on secondary changes in the diaphragmatic and left basal lung shadows. Fixation and elevation of the left diaphragmatic dome, followed by pneumonitis and pleural effusion as the infection spread had been considered the most reliable available indication. Fluoroscopy of the chest for diaphragmatic mobility assumed special importance because the left diaphragm, which is normally freely movable, may be fixed but not necessarily elevated in the presence of subdiaphragmatic pathology.

In 1938, Anspach<sup>1</sup> indicated that separation of the fundus of the stomach from the diaphragm might be a radiologic finding suggestive of left subphrenic abscess. This would be noted if the stomach bubble were separated from the diaphragm, or the fundus could be visualized with barium, and was the first step toward a roentgenologic sign based on the anatomy of the left subdiaphragmatic space.

Soon thereafter Carter<sup>2</sup> specifically described the usefulness of determining the relationship between the left leaf of the diaphragm and the cardia of the stomach by examining the patient in the Trendelenburg position after a barium meal. This maneuver was successfully employed in three of the six patients he reported. Normally, the cardia of the stomach lies in close apposition to the diaphragm. He noted that an abscess in the left anterior subdiaphragmatic space displaced the stomach downward, medially and posteriorly, and one in the posterior space deviated the stomach anteriorly.

The object of this article is to stress that separation of the cardiac end of the stomach and/or the splenic flexure from the diaphragm is a definite radiographic sign in the diagnosing of left subdiaphragmatic pathological conditions.

According to Ochsner and Graves,<sup>3</sup> the left subdiaphragmatic space is divided into three compartments. The *left anterior intraperitoneal space* is bounded by the diaphragm above, adhesions between the stomach or omentum to the anterior abdominal wall below, the left lobe of the liver to the right and below, the spleen to the left, the coronary and falciform ligaments to the right and the left lateral ligament behind. This space is most frequently affected. Abscesses may be localized to smaller areas created by adhesions within the space. It can readily be seen how the relatively yielding upper anterior wall of the stomach might be displaced by a collection between it and the diaphragm.

The *left posterior intraperitoneal space* is the lesser peritoneal sac. This space might be involved by perforation of a gastric ulcer or posterior wall gastric carcinoma.

The *left extraperitoneal space* is the loose areolar tissue which surrounds the kidney, pancreas and descending colon on its posteromesial aspect. Abscesses in this area may follow an infection of the vertebral bodies, a long standing chronic empyema, a perinephric abscess or a perforation of an adherent gastric ulcer posteriorly.

Left subphrenic abscesses occur about one-third as often as on the right. Their diagnosis is difficult, one of the chief reasons being that it is usually overlooked as a possibility in the differential diagnosis. However, not all subphrenic collections are

due to infection. Of the three cases reported here only one was an abscess. The second was caused by a large perforating neoplasm



FIG. 1. Pronounced elevation of diaphragm and mesial displacement of cardiac end of stomach resulting from carcinomatous deposit in the left subdiaphragmatic space secondary to carcinoma of cardia. Note free air in tumor from perforation of necrotic gastric neoplasm. Study made with patient in Trendelenburg position.

of the cardia and the third by a nonspecific granuloma secondary to a minute perforation in the splenic flexure. In the first two cases the diagnosis was established by the separation of the cardia from the diaphragm, and in the third the splenic flexure was definitely depressed.

#### CASE REPORTS

**CASE I.** I. S., a thirty-five-year old man had complained of persistent, dull backache and vague abdominal discomfort for two years. One episode of acute pain had been diagnosed as appendicitis eighteen months before. Appendectomy was performed but no relief of pain followed. Three weeks before admission he first noted tarry stools. Four days before admission there was a large hematemesis with loss of consciousness.

When admitted he was pale but well nourished. His abdomen was tympanitic and there

was slight spasm in the left lower quadrant. A mass which was considered to be an enlarged spleen was felt in the left hypochondriac area.



FIG. 2. Increased opacity of the left subdiaphragmatic area with narrowing and displacement of the cardiac end of the stomach downward and mesially by a subdiaphragmatic abscess. Note the distance between the left diaphragmatic cusp and the upper end of the cardia. Film taken with patient in prone position.

drium. The breath sounds at the left base were diminished. His liver was palpable 5 em. below the costal arch.

Radiographic examination of the chest showed a moderate pleural effusion at the left base. Films taken with the patient in the Trendelenburg position after a barium meal showed a pronounced separation of the diaphragm from the cardiac end of the stomach. At first this was considered to be due to pressure from the supposedly enlarged spleen. The possibility of a large neoplasm at the cardiac end of the stomach was suggested in the x-ray report.

His course was progressively downhill. A clinical diagnosis of hepatosplenomegaly of unknown etiology was made.

At autopsy there was a tremendous carcinoma arising from the cardia. A large mass of neoplastic tissue separating the stomach from the diaphragm was present. It extended

through the left leaf into the lung. On cut section the mass was found to be necrotic and contained a small amount of air. (Fig. 1.)

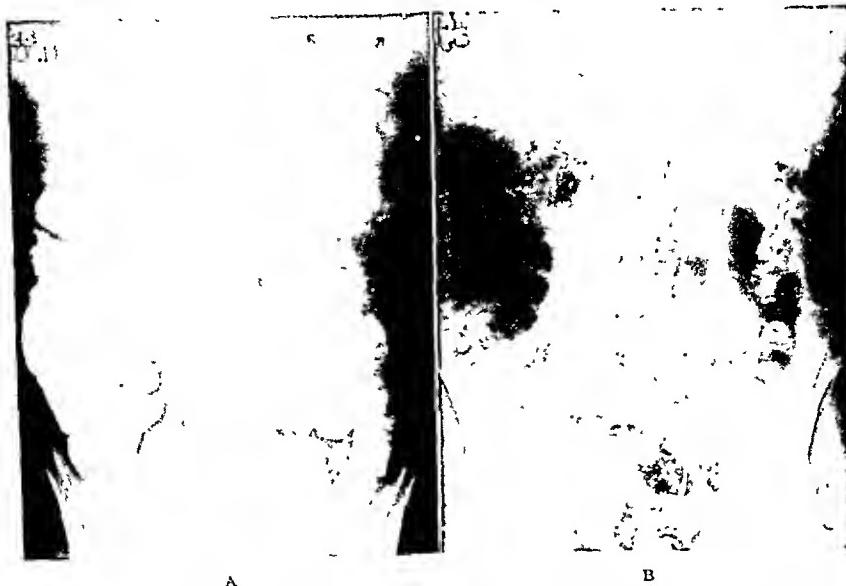


FIG. 3. A, the distal loop of the splenic flexure is depressed by a suprarectal granulomatous mass which fills the subdiaphragmatic space. Note distance between the diaphragm, indicated by arrows, and the splenic flexure. B, barium-air contrast study showing depressed splenic flexure and narrowed lumen of infiltrated distal loop.

**CASE II.** E. H., a sixteen-year old girl had bilateral peritonsillar abscesses during June, 1940. She made an uneventful recovery following incision and drainage. Three months later she was readmitted suffering from severe epigastric and left upper quadrant pain which was attributed to a blow in the left upper abdomen about a week before admission.

The spleen was not palpable when first examined. One week later it was enlarged 2 cm. below the costal margin. Her temperature ranged between 100° and 105°F. accompanied by severe chills. Exquisite tenderness over the upper portion of the abdomen with distention was present. The following week a tender, tense mass was palpated in the left upper quadrant. There was no abdominal rigidity.

Radiographic examination of the chest was normal on admission. Two weeks later a slight haze appeared at the left costophrenic sinus, but the diaphragmatic mobility was unimpeded. The opacity at the left base increased until a well defined pneumonitis and pleural effusion developed. In view of the clinical course and radiographic findings a diagnosis of a left subphrenic pathological disorder was ventured. Soon thereafter an opacity in the left upper quadrant was noted on direct x-ray study of the

abdomen. The patient was given a barium meal and a definite separation of the cardiac end of the stomach from the diaphragm was demon-

strated. A diagnosis of left subdiaphragmatic collection was made.

Subsequently 4 cc. of bloody purulent material was aspirated from the left subdiaphragmatic space. At operation the twelfth left rib was resected revealing a large granulating mass in the subphrenic space within which was an abscess. It was believed to be metastatic from the peritonsillar infection. The patient made an uneventful recovery. (Fig. 2.)

**CASE III.** I. R., a forty-five year old woman had complained of sharp pain in the left lower quadrant radiating to the back four months previous to admission. This disappeared and was followed by a constant dull ache. Two weeks before admission the pain recurred. There was loss of appetite and occasional vomiting. One week later she suddenly became constipated, had intermittent abdominal cramps and evacuated dark red blood clots. She lost fifteen pounds in four months.

Examination revealed a smooth, round, slightly tender, ballotable mass in the left upper quadrant extending 1 cm. below the level of the umbilicus. The liver was palpated 2 cm. below the costal margin. A clinical diagnosis of neoplasm of the kidney or splenic flexure was made.

A retrograde pyelogram showed the left kidney to be normal. A barium enema revealed the splenic flexure to be depressed below the horizontal level of the hepatic flexure. There was a constant filling defect 6 cm. long in the distal loop of the splenic flexure, irregularly narrowing its lumen. The findings were interpreted as indicative of an intrinsic lesion of the bowel, either neoplastic or inflammatory, with possible perforation resulting in a retroperitoneal mass which displaced the splenic flexure downward.

At operation the tumor in the left upper quadrant was found to consist of splenic flexure and an extrinsic mass which extended therefrom toward and involving the transverse colon. It also extended retroperitoneally to the right of the midline. At the junction of the splenic flexure and descending colon, corresponding to the site of the filling defect on the radiogram, the bowel was thickened, friable and inflamed. A Rankin obstructive resection was performed. The pathologic diagnosis was "colon with colitis and nonspecific granulomatous pericol-

tis." The patient made a good recovery. (Figs. 3A and B.)

#### COMMENT

Visualization of the stomach with barium, followed by examination with the patient in the Trendelenburg position, normally demonstrates close apposition between the cardia and the diaphragm. In the presence of a left subdiaphragmatic pathological condition, separation of these two structures can be demonstrated radiographically. Similarly, depression of the splenic flexure may be indicative of left subphrenic disorders, inasmuch as it normally rests close to the left diaphragm and at a higher level than the hepatic.

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# GAS BACILLUS INFECTIONS COMPLICATING SURGERY OF THE UPPER URINARY TRACT

JOSEPH A. LAZARUS, M.D.

Attending Surgeon, Park East Hospital

NEW YORK, NEW YORK

INFECTIONS with the gas bacillus are far from uncommon, particularly in traumatic surgical practice and in surgical procedures carried out upon the gastrointestinal tract. The incidence of this infection occurring as a complication in urologic surgery is much less, and it is particularly small in surgery confined to the upper urinary tract, there being but twenty-four definitely recorded cases including the one about to be described.

## ETIOLOGY

So-called "gas-bacillus" infections may be due to a variety of bacteria. The predominating organism, however, is the *Bacillus welchii*, designated also as *Clostridium welchii* *bacillus aerogenes capsulatus*. This organism was first described by Welch and Nuttall in 1892. *Bacillus welchii* is also known as *Bacillus phlegmone emphysematose* (Fraenkel) and as *Bacillus perfringens* (Veillon and Zuber). Next in frequency to *Bacillus welchii* is the *Vibrio septique* of Pasteur, and finally the *Bacillus edematiens* of Weinberg and Sequin and the *Bacillus hystolyticus*.

## THE ORGANISM AND ITS MODE OF DETECTION

*Bacillus welchii* appears on the stained smear as a large, thick, gram-positive, rod-shaped bacillus. Smears taken from an infected wound may be positive as soon as six hours after the onset of infection, while cultures may be positive within four hours. On the serum agar plate the superficial colony appears moist and circular with

clear cut edges. Stabs made in freshly boiled litmus milk will reveal the growth in twelve to fifteen hours, the milk becoming partially coagulated and giving off an odor of butyric acid. To be effective, media must be fresh and prepared under strict anaerobic standards. The most reliable diagnostic test for this organism is the test introduced by Welch and Nuttall, in which inoculations are made in rabbits. In this test, the animal's blood acts as the culture medium. Rarely do blood cultures become positive, which might be due to the inhibiting influence of the oxygen present in the blood stream.

*Bacillus welchii* has been found in feces, garden soil, dung, room sweepings, glass syringes and in a variety of other sources. It is normally present in the gastrointestinal tract of man and animals without producing gas. These same organisms, however, under abnormal environmental conditions such as intestinal perforation, gangrenous appendicitis or intestinal obstruction may and frequently do take on gas-producing propensities. Cases have been reported in which the *Bacillus welchii* was found in surgically extirpated gall-bladders, the apparently normal vagina, and in wounds presenting no clinical evidence of infection (Kraft, Aschoff). *Bacillus welchii* has also been found present for long intervals outside the gastrointestinal tract without producing gas. In fact, Hendry reported two cases of *Bacillus welchii* infection in which symptoms appeared ten years after the injury occurred, indicating that under certain conditions, such as trauma or surgery, organisms originally possessing a low grade of virulence may

become activated and lead to fulminating sepsis.

#### PATHOLOGY

For *Bacillus welchii* to take root and flourish in a wound, the two prerequisites are a complete absence of oxygen and the presence of devitalized tissue. Both of these conditions are satisfied in a variety of wounds, such as crushing wounds, punctured wounds, lacerations associated with severe injury to adjoining structures, wounds harboring foreign bodies and particularly those carried in from the outside. The usual period of incubation is from one to six days, the average being three days, although infections may appear a few hours after injury or as long as ten years after injury. Structures possessing a good blood supply are less apt to become infected than when the blood supply is limited, as is illustrated by the infrequency of *Bacillus welchii* infections in head and neck injuries. *Bacillus welchii* infections show a marked predilection to spread rapidly along muscle bundles, although they may spread in connective tissue planes and along subcutaneous spaces.

As a rule, this type of infection rarely gives rise to frank pus unless it is complicated by pyogenic organisms. The discharge is serosanguineous in character and presents a characteristic sweetish, mousy odor which, once smelled, is rarely forgotten. The presence of gas bubbles in the tissues is one of the diagnostic features of this infection. Death is due to toxemia rather than to blood invasion, the toxins involved being primarily those resulting from the organisms rather than from tissue degeneration.

#### SYMPTOMS AND DIAGNOSIS

The disease is usually ushered in by an abrupt rise in temperature and by an increase in the pulse rate, the latter being out of all proportion to the elevation in temperature. The respiratory rate is also

increased, which may erroneously lead to the suspicion of a pulmonary complication. Soon after the rise in temperature, the patient complains of pain in and around the region of the wound. Early inspection of such a wound will disclose swelling, with a more or less normal appearance of the skin surrounding the wound edges. Shortly thereafter the skin becomes pale and tense and presents a slightly yellowish tint. Purplish patches frequently follow the yellowish discoloration. These grow larger, frequently coalesce and form blebs containing a serosanguineous fluid with a characteristic sweetish, mousy odor. At a still later stage the purplish color changes to a dirty green. Occasionally, the affected part presents a bronze hue. Palpation reveals a sense of distinct crepitation extending from the wound to the outlying regions of integument. The presence of air in the tissues may be disclosed much sooner by x-ray than by the palpating hand. Positive cultures and smears made from the wound clinch the diagnosis.

#### TREATMENT

As soon as the diagnosis is made, or, better still, suspected, the wound should be laid wide open. The entire involved region should also be exposed by liberal incisions. Muscle planes should be bluntly separated rather than divided. Frequent copious washings with oxygenized antiseptics such as hydrogen peroxide or freshly prepared Dakin solution must be instituted. Serum therapy is highly desirable in this type of treatment and should be started as soon as the organism is found, employing preferably a mixed or polyvalent *perfringens* serum administered locally, subcutaneously and intravenously. The product commonly employed is the one containing 10,000 units of *Vibrio septique* antitoxin in each syringe package. The patient's sensitivity to serum must be ascertained before employing the serum intravenously. X-ray therapy has been employed with good results in early cases.

**ANALYSIS OF TWENTY-FOUR CASES OF GAS  
BACILLUS INFECTION FOLLOWING  
SURGERY OF THE UPPER  
URINARY TRACT**

**Sex.** In five of the twenty-four patients the sex was not stated. Of the remaining nineteen patients, thirteen (68.4 per cent) were males.

**Age.** Of the nineteen patients whose ages were noted in the protocols, there were none listed in the first and second decades, nor after the sixth decade. In the third decade there were five patients, four in the fourth, and five in the fifth and sixth.

**Side Involved.** The side involved was noted in eighteen instances, and of these, the left side was involved in ten patients (56 per cent).

**Organs Involved.** In the total series of twenty-four cases, the kidney was involved in twenty-two patients (91.7 per cent) and the ureter in two (8.3 per cent).

**Preoperative Diagnosis.** There were fourteen operations performed for calculi (58.3 per cent), twelve upon the kidney and two upon the ureter; and in five of these fourteen cases the condition was associated with pyonephrosis. In eleven instances (45.8 per cent) the kidney was the seat of infection, and in five of these the infection was associated with calculi. Three patients were operated upon for tumor (12.5 per cent), two of which were malignant and one benign (renal cysts). The group presents but one instance of hydronephrosis apparently without stone or infection. This was in a patient with a horseshoe kidney (Rathbun), in which one side was hydronephrotic and in which a heminephrectomy was performed.

**Types of Operations Performed (Twenty-one Cases)—(in Three the Procedure Was Not Stated).** Bacillus welchii infection occurred in ten patients following nephrectomy (47.6 per cent), in four instances (19 per cent) following nephrotomy, in four (19 per cent) following pyelotomy, and in two (9.5 per cent) following ureterolithotomy. The simple removal of two cysts

from one kidney was followed by this type of infection in one patient (Mencher and Leiter). It might be mentioned that in this patient a suprapubic cystotomy for hypertrophy of the prostate was also performed at the time of the renal operation.

**Treatment and End Results.** The end results were tabulated in twenty cases, and it is from this group that statistics are computed. There were fourteen patients (70 per cent) who recovered, and six (30 per cent) who died. Of the fourteen patients who recovered, there were ten (71.4 per cent) who received serum along with the routine local treatment, and four (28.6 per cent) who did not. In the group of six patients who succumbed, two died before any treatment could be given, leaving four who died in spite of treatment. These four patients received routine treatment along with polyvalent perfringens serum.

#### CASE REPORT

G. C., male, aged fifty-six, a leather goods worker, complained of left lumbar pain of two years' duration. Save for a bilateral hernioplasty performed fifteen years previously, the past history was entirely irrelevant.

Physical examination revealed a well developed, highly nervous man, fifty-six years of age, who did not appear acutely ill. The two outstanding features of the examination were left costovertebral tenderness and a large boggy prostate. The urine showed a faint trace of albumin and twenty to thirty white blood cells per high power field.

Hemoglobin was 13.4 Gm. per 100 cc. of blood. The Wassermann test was negative.

Cystoscopy, which was performed elsewhere, disclosed a few red blood cells and leukocytes from the left renal specimen. Cultures were sterile.

A flat film of the genitourinary tract disclosed a large calculus about the size of a peanut kernel situated in the lower calyx of the left kidney, and a smaller calculus about the size of a split pea situated in the region of the upper calyx. The left renal silhouette was enlarged.

Under spinal anesthesia the left kidney was exposed through an eight-inch Albaran incision. The organ was enlarged to about one and

a half times the size of normal, and presented a considerable degree of perinephritis. Situated in a dilated lower calyx there was a large fragmented stone aggregating the size of a large peanut kernel.

The kidney was freed from its adhesions, delivered into the wound, carefully surrounded with moist pads, and through a small incision made through the parenchyma just above the lower pole, one of the calculi was palpated and removed in fragments. The calculus in the upper calyx was removed with difficulty through a small incision made through the renal parenchyma just below the upper pole, and supplemented with a small counter incision on the anterior surface of the kidney after fixing the calculus with the tip of the index finger introduced through the larger opening. All wounds were closed with mattress sutures of heavy plain catgut incorporated over pieces of muscle tissue. Over each incision a strip of fat was lightly anchored into place. At no time during the procedure was there any question of entering the peritoneum or of injuring the colon. The wound was closed in layers after draining the renal fossa with one rubber tube and a piece of rubber dam. There was very little loss of blood during the entire operative procedure, and he was returned to his room in excellent condition.

Approximately seven hours after operation the temperature rose to 102°F., the blood pressure dropped to 80/60, the pulse became thready and of poor quality, and the facies assumed an anxious expression. Although he presented many of the features of shock, his skin remained warm. Intravenous drip infusion of glucose and saline was immediately started along with the routine treatment for shock. The following morning he was given 500 cc. of citrated blood, but this failed to produce any appreciable improvement in his general condition. That night the blood pressure was 100/80. Forty-eight hours after operation the temperature rose to 103.4°F., and his skin became slightly icteric, and the pulse imperceptible. Examination of the wound disclosed an enormous edema; and the surrounding skin showed a purplish discoloration extending up to the level of the scapula. There was no evidence of crepitation at this time. The superficial layer of the wound was promptly laid open and a slight amount of seropurulent exudate was evacuated. Tubes were introduced for dakiniza-

tion. The next morning he appeared septic, and distinct crepitation around the wound was elicited. There was a sweetish, mousy odor to the discharge. Smears and cultures showed the presence of *Bacillus welchii*.

Under cyclopropane anesthesia, all layers of the lumbar wound were laid wide open, and long incisions made in the chest wall. Muscle bundles were freely separated as far as the scapula. Free gas bubbles could be seen in the exposed tissues. The wound was inundated with hydrogen peroxide and 12 Gm. of sulfanilamide crystals were placed into the tissues. Polyvalent *perfringens* serum was administered subcutaneously and intravenously, and oxygen given through a BLB\* mask. Although the temperature dropped to 100°F., the patient succumbed the following morning from sepsis. A postmortem examination could not be obtained.

*Comment.* Immediately following the diagnosis of *Bacillus welchii* infection, the bacteriological department made a thorough investigation of all catgut and supplies of the operating room with negative results. No cases of *Bacillus welchii* infection had been seen at this hospital in the past several years. Operations performed subsequently were also uncomplicated, indicating thereby that the infection could not possibly have been contracted in the operating room.

Since it is certain that the intestine was not injured during the course of the nephrolithotomy, this source can definitely be ruled out as playing any role in this case.

In view of the fact that we were dealing here with a patient with a fragmented calculus, it is quite possible that the calculus harbored the *Bacillus welchii* organism, as was evident in the case presented by Ferrier and Bliss, in which bacilli were found in the center of the calculus. Yet, Mencher and Leiter noted the fact that routine bacteriological examinations of renal calculi disclosed three instances of stones which harbored *Bacillus welchii*, but in none of these three patients did the wound become infected. Unfortunately, no bacteriological examination was carried out upon the calculi in this case.

\* Boothby, Lovelace Bulbulian.

## SUMMARY AND CONCLUSIONS

Gas bacillus infections complicating surgery of the upper urinary tract are rare,

tissues recovered from patients who presented no clinical evidence of wound or systemic infections. It has also been found in four renal calculi, but in only one of

TABLE I

Author	Sex	Age	Side	Diagnosis	Operative Treatment	Treatment of Infection	End Result
Howald, R.	Female	34	Left	Tuberculous pyonephrosis	Nephrectomy	H <sub>2</sub> O <sub>2</sub> plus scrum	Recovery
Meyer, A. W.	Male	54	Left	Caleulus pyonephrosis	Nephrectomy	H <sub>2</sub> O <sub>2</sub>	Recovery
Idem	Female	66	Left	Caleulus pyonephrosis	Pyelotomy	H <sub>2</sub> O <sub>2</sub>	Recovery
Idem	?	?	?	Stone	Pyelotomy	H <sub>2</sub> O <sub>2</sub>	Recovery
Idem	?	?	?	Stone	Pyelotomy	H <sub>2</sub> O <sub>2</sub>	Recovery
Turner, B. W.	Male	36	Left	Stone	Nephrolithotomy	H <sub>2</sub> O <sub>2</sub> plus serum	Died
Idem	Female	30	Left	Stone plus cortical abscesses	Nephrectomy	Dakin plus $\gamma$ -ray Rx	Died
Weintraub and Messeloff	?	?	?	Sarcoma of kidney	?	?	?
Doering, H	?	?	?	Pyonephrosis (pus in kidney showed <i>Bacillus welchii</i> )	?	?	?
Idem	?	?	?	Perinephritic abscess	?	?	?
Ferrier and Bliss	Female	40	Left	Stone	Pyelolithotomy	Dakin plus serum	Recovery
Knapper, C.	Male	30	?	Caleulus pyonephrosis	Nephrectomy	No treatment	Died
Rathbun, N. P.	Male	26	Left	Hydronephrosis in horseshoe kidney	Heminephrectomy	Dakin plus serum	Recovery
Lowsley and Hunt	Male	46	Left	Stone	Nephrotomy	H <sub>2</sub> O <sub>2</sub> plus serum	Died
Mencher and Leiter	Male	60	Left	Carcinoma	Nephrectomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Male	60	Right	Stone	Pyelonephrolithotomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Male	36	Right	Tuberculosis and left epididymitis	Nephroureterectomy and left orchidectomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Male	22	Right	Tuberculosis	Nephrectomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Female	42	Right	Caleulus pyonephrosis	Nephrectomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Male	50	Right	Cysts of kidney and hypertrophy prostate	Removal of cysts and suprapubic cystotomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Male	50	Right	Tuberculosis	Nephrectomy	Oxygen plus dakin plus serum	Died
Idem	Male	24	?	Stone in ureter	Pelvie ureterolithotomy	H <sub>2</sub> O <sub>2</sub> plus serum	Recovery
Idem	Female	44	Right	Stone in ureter	Ureterolithotomy	None	Died
Lazarus, J. A.	Male	56	Left	Stones	Nephrolithotomy	H <sub>2</sub> O <sub>2</sub> plus serum plus sulfanilamide plus oxygen	Died

there being but twenty-four definite cases collected from the literature, including the case here presented. Although gas bacillus infections may be due to a variety of organisms, the predominating one is the *Bacillus welchii*. This organism has been found in

these was it associated with wound infection. In this instance the stone was fragmented during its removal.

While the usual incubation period varies from one to six days, the average being three days, it has been known to be as soon

as a few hours after operation, and as long as ten years after inoculation. The outstanding clinical features of this infection are a rise in temperature and pulse rate, marked toxemia, edema and pain in the wound which presents typical purplish discoloration of the surrounding skin, followed later by coalescing blebs. The diagnostic features are crepitation in the subcutaneous tissues, a typical sweetish, mousy odor to the serosanguineous discharge, and positive smears and cultures of *Bacillus welchii*. Smears may be positive within six hours, and cultures four hours after the onset of infection.

Treatment consists of wide open drainage, generous use of oxygenized antiseptic solutions, along with polyvalent perfringens serum. It is quite possible that sulfonamides administered locally and orally may play a great rôle in the future handling of this type of infection. In early cases deep x-ray treatment has given gratifying results. In the collected group, 70 per cent recovered, and of this number, 71.4 per cent received serum. In the group of six patients who succumbed, two died before any treatment could be given, and the remaining four had received serum.

In the entire series of twenty-four cases, the kidney was the source of infection in twenty-two patients (91.7 per cent) and the ureter only twice (8.3 per cent). In 47.6 per cent of the cases the operations preceding the infection were nephrectomies; in 19 per cent nephrotomies; and in 19 per cent pyelotomies. Calculi were present in fourteen patients (58.3 per cent), twelve renal and two ureteral. And in five of these fourteen patients a co-existing pyonephrosis was present. Renal infections necessitating nephrectomies were present in eleven instances (45.8 per cent) and in five cases the infection was associated with calculi.

A case is presented, in which a fulminating *Bacillus welchii* infection followed

nephrolithotomy for calculi, one of which was fragmented. Clinical evidence of infection appeared seven hours after operation.

Although W. M. Miller collected 607 cases of gas bacillus infection, there were only six which followed operations upon the genito-urinary tract. In view of the fact that the type of operation was not mentioned, and no other details available, these six cases are omitted from the series. It is possible that Miller might have included some of the above tabulated cases in his collection.

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# THE MENSTRUAL CYCLE IN THE HUMAN CERVICAL MUCOSA AND ITS CLINICAL SIGNIFICANCE\*

ANTHONY WOLLNER, M.D.

Assistant Professor of Gynecology, New York Post-Graduate Medical School, Columbia University  
NEW YORK, NEW YORK

NINE years ago a systematic histological study of the human cervical mucosa in the intermenstrual period was begun, and observations have been reported in several previous communications.<sup>1,2,3</sup> Characteristic cyclic changes were found in the columnar epithelial elements. These cells cover the endocervix and line the glands. In the early proliferative phase the columnar cells are low, contain little cytoplasm, and they have sharply outlined, regular contours. The nuclei in this menstrual phase are small, deeply stained and are regularly arranged close to the basal membrane. An active proliferation can be observed in this cell type during the intermenstrual period. There is an increase in the number of the cells, they become gradually higher and broader, the cytoplasm increases, the nuclei become larger and elongated, some of them assuming a spindle shape. The nuclei also change their position within the cells, migrating toward the center. At the end of the proliferative phase, signs of accumulating secretion are seen in the cells. In the secretory phase the outline of the individual cells becomes irregular, they are bulging on their surface, and many of them are seen secreting. The nuclei are pale, spindle shaped and densely crowded. Immediately before, or at the beginning of menstruation the columnar cells become exfoliated, which process is rapidly followed by regeneration. The re-epithelization of the surface begins from the base of the glands from where the lining epithelium grows over the denuded surface. The columnar cells covering the surface and those lining the glands take equal part in the cyclic transformation.

Due to the proliferative activity of the columnar cells, the glandular pattern of the cervical mucosa changes in the intermenstrual period. In the early proliferative phase the glands are scanty, widely scattered in a dense, compact stroma. Their outline is regular, on cross section round or oval shaped, on longitudinal section tubular. The lumina are narrow and no secreting columnar cells are seen. In the late proliferative and in the secretory phase the number, size and shape of the glands undergo marked changes. The interglandular stroma becomes less and less, the glands are densely crowded, assume an irregular shape, revealing profuse branching and projections into the surrounding edematous stroma. The lumina become much wider, the lining columnar cells are seen bulging into the lumen and signs of secretion are present. Shortly before and at the onset of menstruation an extensive breakdown of the lining epithelium occurs. Some glands are seen entirely denuded, and after the exfoliation is completed the glands collapse and gradually reassume their regular outline with narrow lumina. A rapid regeneration follows and before the end of the menstrual period the cervical mucosa presents a normal histological picture. The stroma is a dense, fibrous tissue in the early postmenstrual period. The cells are widely spaced, the nuclei are small and there is very little cytoplasm in the stroma cells. The blood vessels are contracted. During the intermenstrual period an increased cellularity is noted, the stroma becomes edematous and loose and the blood vessels are engorged. The stroma cells change their forms and become larger with more cyto-

\* From the Department of Gynecology, New York Post-Graduate Hospital.

plasm. In the secretory phase the stroma simulates an inflammatory condition.

Subsequent histological studies of the

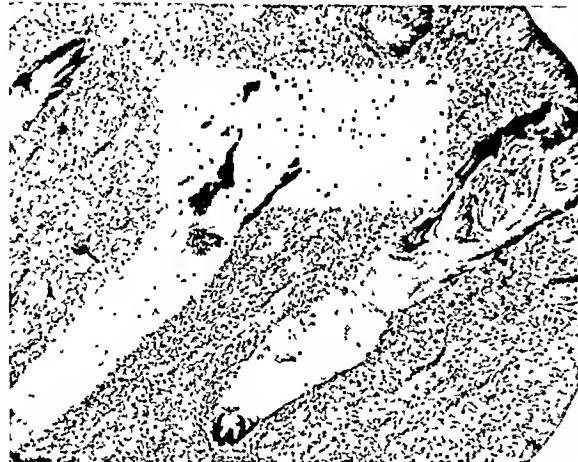


FIG. 1. Collapsed cervical glands partly denuded of their epithelial lining. The right side gland demonstrates the beginning re-epithelialization.

menstrual cycle confirmed these observations. A typical histological cycle could not, however, be observed in all of the cases, but a clear-cut cycle was found, involving uniformly all the tissue elements in about 70 per cent. In 30 per cent an exact determination of the menstrual phase was difficult. In the majority of these cases the cervical mucosa presented a confused histological picture in which glands characteristic of different menstrual phases were seen side by side. A certain overlapping of different histological phases in the same specimen is physiological, since the ovarian hormone action does not result in a uniform and simultaneous change in the mucous membranes. For the determination of the typical menstrual phase, it is essential that a generous piece of tissue be available for histological study. I also found specimens, in which the histological picture did not correspond with the known menstrual date, and believe that such a discrepancy is always suggestive of an imbalanced ovarian action. A normal menstrual history and apparently normal genital organs do not exclude the possibility of an abnormal ovarian function. In the case of anovulatory menstruation no clinical symptom indicates the true condition, except steri-

lity. Persistent Graafian follicles containing active follicular hormones may also be present without initiating clinical symp-



FIG. 2. Almost entirely regenerated cervical gland. The lumen is filled with the exfoliated epithelium.

toms, but the accentuated hormonal action and the absence of a corpus luteum is reflected in the histological pattern of the mucous membranes of the genital tract. An atypical histological cycle in the cervical mucosa is probably caused by ovarian dysfunction.

The cervical mucosa in the physiological menopause or after castration undergoes atrophic changes. The stroma becomes a dense connective tissue with pyknotic cells. The blood vessels are contracted and have unusually thick, muscular walls. The glands are regular in outline and have collapsed lumina. The lining epithelium in some of the glands is completely cast off, while in others the columnar cells reveal signs of pyknosis. Inactivity and gradual disappearance of the columnar epithelium is the outstanding feature in the cervical mucosa after the cessation of ovarian function. In physiological menopause, since the ovarian hormone production may continue for a long while after the cessation of menstruation, remnants of active columnar cells may be found in the mucosa many years after the clinical onset of the menopause. After surgical castration, however, the atrophic changes progress rapidly.

After my reports on the histological cycle, Sjövall<sup>4</sup> investigated human cervices removed by surgical operations or at

such as myomas and carcinomas, do not influence the normal cycle, is contrary to my observations. I firmly believe, that

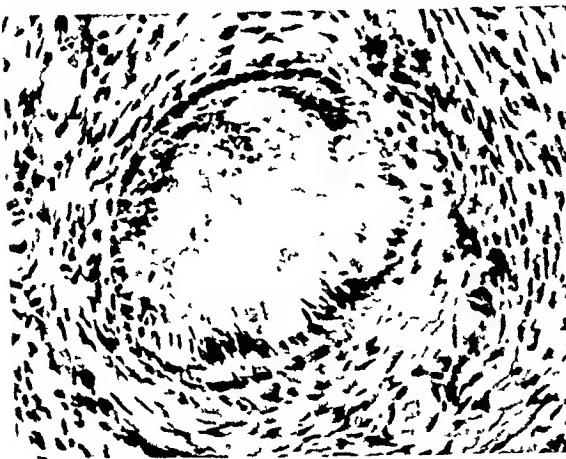


FIG. 3. Cross section of a cervical gland demonstrating a simultaneous process of exfoliation and regeneration.



FIG. 4. Cervical stroma with engorged blood vessels, some of which opened up on the surface.

autopsies. He studied the cyclic changes in thirty-four cervical specimens, nine of which were obtained at autopsies, six after supravaginal hysterectomies and sixteen from cases in which cervical biopsy was indicated by some cervical pathological condition. His conclusions were, that the human cervical mucosa is under ovarian hormonal influence, like the rest of the genital tract. He believes, that the proliferation of the columnar cells culminates in the early secretory phase and not later as described by the author. He was unable to ascertain a tissue loss at the time of menstruation. According to his observations, the cyclic transformation in the cervical mucosa is synchronous with the changes in the endometrium and in the ovaries. In eight cases of secondary amenorrhea with atrophied endometria, and in fourteen cases of cystic glandular hyperplasia of the endometrium he found identical histological changes in the endocervix. In childhood and after the menopause he found the cervical mucosa inactive.

Sjövall's description of the histological cycle can not be accepted in all its details without certain reservations. His specimens were obtained from pathological material, and his contention, that genital diseases,

conclusive data of the normal cycle can be obtained only by the study of cervical specimens taken from normally menstruating women with apparently normal genitalia.

The loss of tissue incidental to menstruation was demonstrated in previous papers. In an additional four cases, in which a cervical specimen was secured from normal women immediately before or during the menstrual flow, I subjected the specimens to a painstaking histological study on serial sections. One specimen was obtained one day before the expected menstrual date. The serial sections revealed an overwhelmingly late secretory phase, but some glands were seen in the process of exfoliation and simultaneous regeneration. This observation seems to indicate that exfoliation and regeneration may begin in the mucous membrane before the clinical onset of menstruation. In two cases cervical specimens were taken at the beginning of the menstrual flow. Both specimens presented a similar histological picture. Extensive loss of tissue was noted in the cervical glands. In the serial sections, glands typical of the late secretory phase were found side by side with exfoliating, completely denuded and regenerating glands.

In the edematous stroma enormously dilated blood vessels filled with erythrocytes were seen. Blood was also found in the lumina of the glands, accompanying the process of exfoliation. In the fourth case, the cervical specimen was obtained on the third day of the menstrual flow. The mucosa revealed a completely regenerated histological structure. It is evident, therefore, that the process of exfoliation and regeneration is completed in the cervical mucosa before the end of the clinical menstruation.

The following photomicrographs illustrate some recent observations. They were taken from different sections of the same specimen, obtained on the first day of menstruation. Figure 1 demonstrates glands partly denuded, with the lining epithelium still clinging to the surface in some areas. Erythrocytes are seen in the lumen of the glands. In the gland on the right side of the picture regenerating epithelium is seen in a small area, revealing numerous mitoses. Figure 2 is the picture of an almost entirely regenerated gland. In some areas, however, the lining epithelium is still in the process of exfoliation, and the lumen is filled with desquamated epithelium. Figure 3 demonstrates the cross section of a gland under high power. It shows the simultaneous process of exfoliation and regeneration within the gland. Figure 4 includes a part of the stroma with engorged blood vessels, one of which is opened up on the surface. The surface epithelium is exfoliated.

The author's personal histological observations incidental to menstruation can be summarized as follows: Immediately before and at the beginning of menstruation there is an extensive loss of tissue in the cervical mucosa involving the columnar epithelial elements. Exfoliation and regeneration occurs simultaneously in the glands, and with such rapidity, that the process is probably completed within twenty-four hours. Before the end of the menstrual flow an entirely regenerated mucous membrane is present. The destructive process is accompanied by bleeding.

Free blood is found in the lumina of the exfoliating glands, and some of the tremendously dilated blood vessels near the surface are seen opened up after the exfoliation of the surface epithelium. This observation seems to indicate that the cervical mucosa contributes to the loss of blood during the menstrual flow.

Since the ovarian hormones govern the biological function of the human cervical mucosa, an investigation of the possible rôle of these hormones in the production of pathological changes is indicated. The most frequent cervical pathologic alteration is endocervicitis. The clinical diagnosis of this condition is based on the presence of a copious discharge from the cervical canal. Histologically, endocervicitis is characterized by an abundance of secreting cervical glands, and the amount of discharge is proportionate to the number of the glands. The development of the glandular structure in the endocervix is dependent upon the follicular hormone action. In the normal menstrual cycle, concomitant with the increasing hormone production in the ovaries, a gradual increase in the number and size of the cervical glands is noted. This observation was confirmed by Sjövall.<sup>4</sup> In cases with hypofunctioning ovaries an underdeveloped glandular structure is found in the endocervix, and in these cases cervical discharge is either entirely absent or scanty. After the cessation of ovarian function the cervix becomes atrophic and dry. In a series of castrated women I was able to reactivate the atrophic cervical mucosa by the administration of estrogen.<sup>5</sup> The columnar cells were stimulated to new growth, and by the administration of large doses of estrogen glandular hyperplasia with the clinical symptoms of leukorrhea was produced in the inactive endocervix. Zondek<sup>6</sup> followed up the cervical changes in three patients after the administration of large doses of estrogen, and found in all of his cases a remarkable increase in the number and size of the glands. The results of ovarian hyperfunction are known as glandular hyperplasia in the endometrium.

Similar changes were observed in the cervical mucosa with resulting symptoms of cervical discharge.

Erosion, clinically, is a red area around the external os, simulating an inflammatory condition. Histologically, this area is covered with columnar epithelium which is an extension of the endocervical surface epithelium. The occurrence of cervical erosions is fairly constant from the time of birth to the age of menopause, irrespective of infections. After the cessation of ovarian function they gradually disappear. In two menopausal women, who received moderate doses of estrogen continuously over fourteen and eighteen months, respectively, I observed the gradual development of an erosion in the dry, atrophic cervix. After the discontinuance of the hormonal treatment these erosions completely disappeared. Zondek<sup>6</sup> reported in one case the production of a large, partly papillary erosion after the administration of large doses of estrogen. He believes that an erosion of the portio can be caused by hormonal irritation.

Endocervicitis and cervical erosion can be produced in women by excessive hormonal stimulation. It is erroneous, therefore, to regard these cervical changes indiscriminately as the result of an infection. My clinical and histological observations indicate that glandular hyperplasia in the endocervix, and an active proliferation of the endocervical surface epithelium onto the portio, both caused by hormonal irritation, favor the invasion of infectious agents into this structure. Consequently, these hormonal derangements are frequently associated with infection. There are numerous cases, however, in which infection is absent, and the clinical syndrome of endocervicitis and cervical erosion is present only as the manifestation of a hormonal dysfunction.

Atypical epithelial proliferations may be initiated in the human cervical mucosa by hormonal irritation.<sup>7</sup> Up to the present time epithelial metaplasia was interpreted in the endocervix as a healing phase in

erosions. The theory was, that the squamous epithelium growing back to the denuded surface, in its proliferation surrounds and invades the ducts of the glands. It was also believed that this invasive growth eventually becomes displaced to the surface where it belongs after the healing process is completed. My histological observations in a great number of erosion cases do not seem to substantiate this conception. If the healing process were the etiological factor for epithelial metaplasia, we should be able to find this histological picture in almost every case of erosion. In my material, however, I found it only in rare instances. In a series of castrated women I was able to produce epithelial metaplasia in dry, atrophic cervices by hormonal stimulation.<sup>7</sup> The importance of the hormonal etiology of epithelial metaplasia lies in this pathological condition's possible relationship to the development of carcinoma. Investigations into early cases of cervical carcinoma which were subjected to a painstaking histological study on serial sections, suggest that atypical epithelial proliferations probably present the first developmental phase in carcinoma.<sup>8,9,10</sup>

#### CONCLUSIONS

Extensive studies on the human cervical mucosa ascertained a histological cycle in this structure which is similar to that observed in the endometrium. The results of these experimental studies suggest that hormones play an important rôle in the production of those cervical disorders, the etiology of which is now obscure.

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# METABOLIC EFFECTS OF THE ANESTHETIC AGENTS\*

SAMUEL ROCHBERG, M.D. AND VIRGINIA APGAR, M.D.  
NEW YORK, NEW YORK

BEFORE the anesthetist puts his patient to sleep, it is important that he know what effect the drug or drugs he is going to use will have upon that particular individual's metabolism both during and after the operation. It is the duty of the anesthetist to maintain the physiological "status quo" of his patient. It is with these thoughts in mind that we present the following review of the literature.

## BASAL METABOLIC RATE

McKesson and Clement<sup>42</sup> have brought forth inadequate evidence from experimental work on the dog and from observations in man that the metabolic rate is very depressed by ether, less by nitrous oxide and least by ethylene.

Tribromethanol (avertin), in moderate doses, lowers the metabolic rate about 15 per cent<sup>27</sup> and, therefore, may be helpful in bringing the metabolic rate closer to normal values in cases of hyperthyroidism and marked apprehension.

It is imperative for the anesthetist to remember that an increased metabolic rate (seen with fever, pain, fear, hyperthyroidism, alcoholism, pregnancy and in young muscular adults) goes hand in hand with increased oxygen consumption and oxygen need. He should also be alert to the danger of anesthetic overdosage in patients with a subnormal metabolic rate (in the very young and very old, hypothyroidism, cachexia, prolonged illness, severe anemia, shock, jaundice and obesity).

## BODY TEMPERATURE

Watkins and Wilson<sup>86</sup> anesthetized twenty-seven patients with ether administered by the open drop method, and found

that eight minutes after the induction began the rectal temperature began to fall; the most rapid fall was in the first thirty minutes. The average fall was 1.8° F. during the first hour, and 0.8° the next hour. They noticed that the temperature fall was more rapid if the anesthesia was light. In the very ill patients, the temperature tended to rise toward the end of surgery.

Under ethylene anesthesia there is a very slight temperature decrease.<sup>7</sup>

Avertin produces a fall in body temperature,<sup>27</sup> which fits in with the picture of general metabolic depression that is produced by this drug. Furthermore, in 1894, Harnack and Meyer<sup>28</sup> reported that amyleno hydrate, in which avertin is dissolved, also lowers the body temperature.

Evipal lowers the temperature.<sup>33</sup>

Heat may also be lost by allowing the expired air to escape into the room, which occurs when anesthetics are administered by the open drop method. This factor is negligible when the closed absorption system is used. Too much exposure of the skin and an increase in peripheral blood flow result in heat loss through radiation. Depletion of the glycogen reserve and circulatory depression lead to diminished heat production.<sup>5</sup>

## LIVER

✓ *Ether.* Liver function tests show that during ether anesthesia hepatic function is diminished, but returns to normal within twenty-four hours.<sup>1,71</sup> Almost always we find a hyperglycemia occurring, and the blood sugar level may rise to two or three times its normal value, the greatest rise occurring during the first hour. There is increased glycogenolysis in the liver, and probably an inhibition of insulin activity. This marked hyperglycemia is closely

\* From the Division of Anesthesia, Department of Surgery, Presbyterian Hospital, New York City.

related to the amount of epinephrine being secreted and stimulation of the sympathetic nerves to the liver, for section of the hepatic nerves or adrenalectomy prevents almost completely a rise in the blood sugar.<sup>52</sup>

In both man<sup>1</sup> and in laboratory animals<sup>49</sup> the secretion of bile is depressed by ether anesthesia, though an occasional animal may secrete bile copiously.

Adriani<sup>1</sup> states that urea formation is normal under ether anesthesia, unless liver damage is present, which results in increased urea formation. However, Bollman<sup>6</sup> and Mann<sup>48,49</sup> claim that there is a moderate increase in urea formation which is in evidence in both the blood and urine. Moreover, the production of urea is not depressed, even in a severely damaged liver, because only a very small amount of hepatic tissue can produce large quantities of urea.

The activity of the reticular endothelial cells (Kupfer cells) is also depressed.<sup>1</sup>

*Chloroform.* Rosenthal and Bourne,<sup>71</sup> using bromsulfalein dye, tested the hepatic function of dogs after chloroform had been administered for only thirty minutes and found that impaired elimination of the dye could be detected for eight days. If chloroform were given for two hours, elimination was subnormal for six weeks.

The elevation of the blood sugar is greater with chloroform than with ether, and it is suggested<sup>15</sup> that this may be due to some extent to the direct action of the drug on the hepatic cells. Within the first half hour the hepatic glycogen is three-fourths depleted. However, the blood sugar level is again normal within twenty-four hours.

Acute fatty degeneration of the liver, heart, kidneys and other organs may follow prolonged chloroform anesthesia. Within a few days the patient may become very ill, have severe nausea and vomiting, become jaundiced, and then lapse into coma. This clinical picture of "delayed chloroform poisoning" or "postanesthetic toxemia" is usually ended by death. These symptoms

develop from the first to the third post-operative day, and the laboratory findings show a severe toxic hepatitis. Due to the failure of prothrombin formation by the injured liver a hemorrhagic tendency is also seen. At autopsy a hepatic necrosis about the central vein is found.<sup>27</sup> If the patient recovers, no residual liver damage is observed, due to the tremendous regenerative powers of the liver cells and not to the choice of anesthetic agent.

This picture of chloroform poisoning can be prevented to some extent by adequate oxygenation during the course of the anesthesia and by a high carbohydrate, high protein and low fat diet prior to anesthesia. Goldschmidt, Vars and Ravdin,<sup>26</sup> and Miller and Whipple<sup>55</sup> believe that the best protection is given by a plenitude of protein stored in the liver.

*Divinyl Ether (Vinethene).* Though vinethene is less toxic than chloroform, it can also produce central lobular necrosis of the liver.

Goldschmidt and his associates<sup>24</sup> state that "the duration of the divinyl ether anesthesia was thus found to be a definite factor in the production of liver necrosis in the dog." They<sup>25</sup> also showed that oxygen lack during vinethene anesthesia contributes in great measure to hepatic damage. Ravdin and this same group<sup>66</sup> have emphasized that if vinethene is given with oxygen in cases lasting over forty-five minutes, no liver damage occurs.

However, Orth and his associates<sup>60</sup> have shown in dogs that prolonged usage or frequently repeated short anesthesias with divinyl ether will produce liver damage in spite of adequate oxygenation. This group reported, in 1941,<sup>30</sup> a toxic hepatorenal syndrome in a patient following the second of two administrations of vinethene that were ten weeks apart and lasted forty minutes and 104 minutes, respectively.

From the above evidence it appears that the liver can be safeguarded during vinethene anesthesia by using it only for short cases,<sup>51,66,67</sup> avoiding repeated usage on the same patient, adequate oxygen and a high

carbohydrate, high protein and low fat intake prior to anesthesia.<sup>26</sup>

*Ethyl Chloride.* Ethyl chloride is a halogen containing hydrocarbon, and therefore is capable of damaging parenchymatous organs. However, the drug does not have a widespread usage, and when employed it is only for very brief cases.

*Ethylene and Nitrous Oxide.* These drugs do not depress liver function or harm hepatic tissue unless anoxia is present.<sup>1</sup>

*Cyclopropane.* Raginsky and Bourne<sup>65</sup> have shown that cyclopropane does not diminish the functional capacity of the liver.

*Tribromethanol (Avertin).* Coleman,<sup>16</sup> using bromsulfalein dye tests, reported that hepatic function is diminished more frequently with avertin than with nitrous oxide or ether anesthesia.

Avertin combines with glycuronic acid in the liver and is excreted by the kidneys. There is little serious effect seen from the doses used in basal anesthesia. However, if liver damage is already present, the conjugating rôle played by the liver assumes very great importance. Beecher's<sup>5</sup> perfusion experiments portrayed this very clearly: a 420 Gm. normal dog's liver reduced the blood concentration of avertin from 130 mg. per cent to 6 mg. per cent in ninety minutes, but a liver in which fatty degeneration was produced experimentally was only one-half as efficient. The same is seen clinically when dangerously prolonged anesthesia results from avertin used in patients with known liver damage.

Adriani<sup>1</sup> states that cloudy swelling is the only pathological change, and Bourne and Raginsky<sup>11</sup> observed in animals that large repeated doses are required to produce hepatic damage, which is only moderate in degree and reversible.

Kobayashi<sup>35</sup> found a marked increase in the bile flow of dogs under both avertin anesthesia and avertin amnesia or sedation. Epinephrine, insulin, atropine, blockade of the reticulo-endothelial system, and concentrated glucose solution given orally did not influence the bile flow. Therefore, he

concluded that the augmented bile flow was the result of the direct action of the avertin upon the liver cells.

*Barbiturates.* Anesthetic doses of the barbiturates decrease liver function and decrease the liver glycogen.<sup>1</sup> However, Atnan and Fenz<sup>2</sup> report that evipal does not produce any disturbance of the blood sugar in diabetics.

It is believed that the comparatively brief anesthesia produced by a single dose of an ultrashort acting barbiturate is due to the rapid side chain oxidation of the drug in the liver. However, the proof that these drugs are destroyed in the liver is all indirect. Patients with poor liver function have remained anesthetized for many hours from a dose of evipal which in normal individuals results in only fifteen minutes of anesthesia. Kopppanyi and his associates<sup>36</sup> have shown that rabbits and cats who were given pentobarbital and phenobarbital twenty-four hours following recovery from two hours of chloroform anesthesia, remained deeply depressed for a long time; occasionally, some of the animals died from doses that were only one-half the average fatal dose. Similar results have been obtained with evipal in dogs.<sup>50</sup>

Reynolds and Veal<sup>69,70</sup> state that the continued administration of pentothal to animals in doses just adequate to maintain light anesthesia will eventually produce signs of heart muscle poisoning and circulatory collapse. The first dose of pentothal produces a few minutes of anesthesia, and subsequent doses, given before complete recovery, result in lengthening periods of anesthesia indicating that the drug is cumulative and is not rapidly and completely destroyed. Kozelka and Hines<sup>37</sup> have confirmed this work. Furthermore, in studying the chemical fate of pentothal in the body, they were unable to demonstrate the drug in the tissues after ten minutes. Pentothal and its oxygen analogue, pentobarbital, could not be shown even during profound depression. If enough pentobarbital had been given to produce a simi-

lar degree of anesthesia, the drug could have been found in the tissues. They, therefore, conclude that pentothal produces its cumulative effects through the accumulation of some unrecognized degradation product.

We can only surmise from the above that barbiturate anesthesia and the liver are closely related, but that the exact mechanism is not known.

*Procaine.* Thieulin<sup>78</sup> found that procaine is converted into para-aminobenzoic acid and di-ethyl-amino-ethyl alcohol. Very little procaine is excreted as such by the kidney, and it is believed that almost all of it is detoxified in the liver.<sup>29</sup> Ellinger and Hof,<sup>21</sup> working with the belief that the liver is the site of detoxication, produced hepatic damage in cats with chloroform, and then showed that these cats had greater susceptibility to intravenous procaine than the healthy controls.

Dunlop<sup>20</sup> observed in dogs that procaine, when injected into the blood stream, is rapidly broken down into nontoxic end products which are slowly excreted by the kidneys, and that though many tissues possess the ability to detoxify procaine, none can do it as quickly as the liver. He, therefore, believes that there are theoretical grounds against the use of large amounts of procaine in patients with severe liver damage.

#### KIDNEY

Beecher<sup>5</sup> states that anoxia rapidly damages the colloidal membrane of the kidney, the glomerular epithelium, and allows it to become permeable to protein, albumin and blood; that an increase in both general arterial pressure and renal blood flow (seen with carbon dioxide excess and oxygen lack) results in an increase in urine formation; that a marked blood pressure fall may greatly diminish urine secretion, and occasionally stop it entirely.

*Ether.* Urine formation is depressed in varying degrees by ether anesthesia. Pringle<sup>64</sup> and Walton,<sup>83</sup> in humans and dogs, respectively, have shown that the

production of urine is inhibited by ether anesthesia. In 335 patients who were undergoing operation and were anesthetized with ether, Miller and Cabot<sup>56</sup> observed that the efficiency of phenolsulfonphalein excretion was decreased on an average of 18.8 per cent, and that excretion returned to normal in twenty-four to forty-eight hours.

Ether is believed to be a sympathetic stimulant, and it is possible that constriction of the renal vessels is the cause of the diminished urine output. In animals that have undergone unilateral renal sympathectomy, the denervated kidney excretes as well under ether anesthesia as when the animal is awake, but the output of the intact kidney decreases.<sup>5</sup>

MacNider has done some classical work on the effect of ether anesthesia on urine formation. He found<sup>43</sup> that when anuria occurred in animals under ether anesthesia, it was a temporary anuria which occasionally became permanent, it occurred one to two hours after the beginning of anesthesia, and it was frequently accompanied by a drop in the blood pressure. The administration of either normal saline or 1 per cent theobromine solution re-established the urine flow. He also showed that age is an important factor. Both young and young adult dogs showed only a very slight impairment of urine formation when anesthetized with ether for two hours. However, the older animals, after one hour of etherization, showed either an oliguria or an anuria with the urine containing albumin and casts. Furthermore, the alkali reserve of the blood was reduced, whereas it was unchanged in the younger dogs.

Upon further study, MacNider<sup>44</sup> discovered that in the renal epithelium and in the glomerular capillaries of the older dogs there was present much more stainable lipoid material. To rectify the disturbance of the acid-base balance, dilute sodium bicarbonate or glucose solutions were given intravenously prior to anesthesia;<sup>45</sup> and it was found from biopsies taken under local anesthesia that the amount of lipoid substance was greatly diminished. After

such intravenous therapy the older animals could be anesthetized with ether for two hours without showing any signs of kidney damage or dysfunction. An increase of lipoid material within the renal epithelium of pregnant animals also seems to be the cause of their susceptibility to ether.

Nitrogen excretion is increased for twenty-four to forty-eight hours after ether anesthesia.<sup>31</sup> The phosphorous output rises,<sup>8</sup> as does the amount of ascorbic acid that is excreted. Glycosuria and ketonuria are frequently present.

*Chloroform.* MacNider<sup>43, 46, 47</sup> found that by the time the induction with chloroform was complete, the dogs were frequently anuric, and by the end of the first hour all the dogs had anuria. A notable decrease in the alkali reserve of the blood was frequently present, and here the use of diuretic solutions were of no avail in inducing a flow of urine.

Upon studying the effect of a two-hour chloroform anesthesia on pregnant dogs, MacNider<sup>46</sup> observed that a preliminary injection of glucose failed to afford any protection, and that the effects were more harmful in the older animals and in the more advanced pregnancies. The tubular epithelium suffers most of the damage,<sup>43</sup> and occasionally hemorrhages are found. Similar changes are seen in the human kidneys.<sup>32</sup>

In man the excretion of urea, uric acid, creatinine and ammonia is increased, but hippuric acid is decreased.<sup>31</sup>

*Cyclopropane.* Waters and Schmidt<sup>84</sup> have shown that cyclopropane depresses renal function only temporarily, and that this is followed by a compensatory increase of short duration.

*Divinyl Ether.* Vinethene anesthesia results in a progressive diminution of renal activity in dogs and may go on to complete anuria.<sup>60</sup>

*Tribromethanol.* In 1931, Veal and his associates<sup>82</sup> noted that in normal rabbits there was a large margin of safety in an anesthetic dose of avertin; but if a very mild nephritis is produced first, the margin

of safety disappears. This may be due to renal failure in eliminating the tribromethanol glycuronate formed in the liver.

Avertin seems to depress urine formation,<sup>14</sup> but does not damage the normal kidney,<sup>58</sup> though 14 to 20 per cent of the patients may show a transient albuminuria.

Under avertin-nitrous oxide-oxygen anesthesia the blood urea rises about 3.4 mg. per cent,<sup>5</sup> but goes much higher in older patients.<sup>63</sup>

*Ethylene and Nitrous Oxide.* Unless anoxia is present, renal activity is not altered.<sup>1</sup>

✓ *Barbiturates.* Large doses of barbiturates produce an antidiuretic effect due to action centrally on the hypophyseal-pituitary system.<sup>27</sup>

Those barbiturates which are not broken down in the liver are eliminated by the kidneys. Since renal excretion occurs rather slowly, those drugs (barbital, phenobarbital) which depend upon the kidneys for elimination, manifest a longer duration of activity. Hence, when renal function is impaired, these long acting barbiturates may cause severe depression and poisoning.

#### GASTROINTESTINAL TRACT

During the induction of anesthesia the odor and taste of the drug may produce salivation, nausea and vomiting. The emesis may be due to the irritating action of the anesthetic agent on the gastric mucosa.

Payer<sup>61</sup> noticed in humans that after anesthesia almost all cases showed some amount of gastric dilatation. In uncomplicated cases this dilatation lasts from twelve to twenty-four hours even though no symptoms may be present. However, when gastric symptoms are present, the stomach is also found to be relaxed for several days.

✓ *Ether.* Experimental and clinical evidence points to ether anesthesia as being a cause of postoperative gastrointestinal symptoms. Beecher<sup>5</sup> states: "In the surgical stage of ether anesthesia almost com-

plete inhibition of the smaller contractions occurs; peristalsis is entirely abolished in the stomach, small intestines, and colon. A distinct loss of muscular tone occurs in these regions."

*Chloroform.* The effects of chloroform are similar to those of ether, but, in addition, there is a tendency to bleed into the serous membranes.<sup>32</sup>

*Ethylene.* There is very little effect produced on the gastrointestinal tract by ethylene and oxygen anesthesia.<sup>53,54,61</sup>

*Nitrous Oxide.* This agent does not seem to alter gastrointestinal activity. However, if anoxia is present an increase in the size of the contractions of the stomach, ileum, and colon (dogs) follows.<sup>53,54</sup>

*Divinyl Ether.* Molitor<sup>57</sup> believes that vinethene does not interfere with the automatic movements of the intestines. However, Burstein<sup>16</sup> has shown in dogs, and the work has been confirmed by Orth et al.,<sup>60</sup> that vinethene diminishes gastrointestinal muscular tone and inhibits intestinal contractions completely in all planes of surgical anesthesia.

*Cyclopropane.* During anesthesia with cyclopropane the intestines are contracted and active, which may be due to the possibility that this agent is a parasympathetic stimulant.

Waters<sup>85</sup> analyzed 10,638 cases and found the incidence of postoperative distention to be as follows: nitrous oxide, 3 per cent; ethylene, 7 per cent; cyclopropane, 13.5 per cent; ether 16.5 per cent.

*Barbiturates.* The barbiturates seem to decrease the intestinal activity, but this is not believed to be as marked as with ether.

#### PANCREAS

Zucker and his associates<sup>87</sup> studied the blood amylase in man under anesthesia and found that ether produced a rise to two or three times the normal value. However, the blood amylase became normal within twenty-four hours.

Avertin did not produce any change in the blood amylase.<sup>87</sup>

#### SPLEEN

Under ether anesthesia the intact spleen of the dog decreases in volume as much as 50 per cent.<sup>4,22,72,73,74</sup> However, the denervated spleen does not constrict, showing that the sympathetic nervous system does play a major rôle in maintaining the splenic volume. This is also implied when the spleen of the dog increases to four or five times its normal size under spinal anesthesia.<sup>17</sup> The variations in the blood pressure and the depth of the anesthesia are also important in controlling the size of the spleen.

All evidence points to the barbiturates as causing splenic dilatation.<sup>22,72,73,74</sup>

#### BLOOD

*Leucocytes.* The father of modern physiology, Claude Bernard, first discovered that anesthesia produces a leucocytosis. All the agents raise the white count, and this is most marked with ether<sup>23,52</sup> and cyclopropane.<sup>77</sup> The total white count rises, and the differential count shifts greatly to the left. The increase in the white blood cells begins with the anesthetic induction and attains a peak in four to eight hours, at which time, depending upon the duration of the anesthesia, it may be two or three times the original count; furthermore, it is three to five days before the count returns to its normal level.

Boyd<sup>12,13</sup> showed that ether anesthesia diminishes the phospholipid content of the leucocytes, indicating that there is a chemical difference between the leucocytosis of disease and anesthesia.

*Erythrocytes and Hemoglobin.* The red blood cell count, the hemoglobin concentration and the hematocrit value increase under ether anesthesia.<sup>72</sup> Essex et al.<sup>22</sup> believe that this is due to the erythrocytes which are injected into the circulation by the profound contraction of the spleen; splenectomy abolishes this blood concentration. The reduction in plasma volume is another cause for the hemoconcentration.

Ether also increases the sedimentation rate of the red blood cells.<sup>38</sup> The platelets are increased by 78,000 per cu. mm. of blood in dogs.<sup>72</sup>

Cyclopropane does not effect the erythrocyte count.<sup>77,84</sup>

According to Bruger and his coworkers,<sup>14</sup> avertin produces a slight rise in the red cell count in dogs. However, Tiba<sup>79,80</sup> claims that there is a 70 per cent decrease in the red count after thirty minutes of avertin and that the sedimentation rate is decreased.

The barbiturates produce a marked dilatation of the spleen and a dilution of the red blood cells which may be sequestered in that organ.<sup>10,22,72,73,74</sup> Dallemande,<sup>18</sup> while working on dogs observed a severe anemia and a fall in the oxygen carrying capacity of the blood from 21 to 9 volumes per cent as late as twenty-four hours after the use of evipal. With repeated anesthesias the anemia became aggravated. As yet, however, there has not been any confirmation of this work in man.

*Blood Volume and Water Balance.* McAllister<sup>40,41</sup> has shown in dogs that ether anesthesia causes a reduction in the blood plasma volume but no marked changes in intracellular or extracellular water. Stewart<sup>76</sup> has found an average reduction of blood plasma volume of 14.3 per cent in humans under ether anesthesia. However, Barbour<sup>3</sup> found no change in the plasma concentration in two carefully controlled periods of ether anesthesia in two rabbits, and, therefore, he believes that ether anesthesia need not produce water shifts into or out of the blood. This does not agree with McAllister<sup>40,41</sup> and Stewart,<sup>76</sup> but the difference may be due entirely to the different animals used in the experiments. We do know that etherization produces hemococoncentration which probably follows the extrusion of erythrocytes from the spleen into the circulation.<sup>4,22,72,73,74</sup>

The barbiturates cause a decrease in the concentration of the blood. This is due to the movement of some of the red blood

cells into the spleen and the addition of a great deal of water to the plasma, most of it coming from the intracellular fluids with the cerebral cortex and liver making large contributions.<sup>3</sup>

The gas anesthetics apparently do not cause any great shifting of the body water. However, with third plane and deeper anesthesia, the reflexes controlling water balance, blood volume and heat regulation may be obliterated;<sup>3</sup> consequently, the physiology of these mechanisms becomes pathological.

*Acid-base Balance.* There is no agreement among the men who have worked on this subject as to what occurs to the acid-base equilibrium during anesthesia. However, the opinion of most is that an acidemia is produced by general anesthesia.<sup>81</sup> Dallemande<sup>19</sup> after an extensive review of the subject concludes that "no law governs the variations of the acid-base equilibrium after the administration of anesthetics."

*Cholesterol.* A rise in the blood cholesterol of 50 to 100 per cent occurs during ether anesthesia, the increase paralleling the duration of the anesthesia, until a peak is reached in sixty to ninety minutes. The values return to normal in four to five hours. This increment in the blood cholesterol goes hand-in-hand with the rise in the blood sugar; however, both substances will remain at almost normal levels if insulin is given several hours prior to the anesthetic. In diabetics though, there does not exist such a relationship between the blood cholesterol and glucose.<sup>5</sup>

Chloroform produces a 5 to 10 per cent rise.<sup>5</sup>

Ethylene, nitrous oxide and the barbiturates do not produce any rise unless the patient undergoes an excitement stage.<sup>5</sup>

*Nonprotein Nitrogen.* The blood urea increases slightly under ether and chloroform anesthesia.<sup>6,34,48,49</sup> The blood ammonia increases 10 to 50 per cent under ether.<sup>74</sup> Cyclopropane does not produce any changes.<sup>50</sup>

## CONCLUSIONS

It is obvious that rarely is there a need for chloroform in the anesthetist's armamentarium, because of its dangerous metabolic effects. Ether, which is supposed to be our safest anesthetic agent, produces marked metabolic disturbances, which, though only temporary in nature, may be most harmful to the very ill patient. Of great importance is the fact that cyclopropane is almost innocuous to the body metabolism.

When vinethene or chloroform are administered by the open drop method, the patients should be given additional oxygen by either the oral or nasal route. Vinethene should not be used for long procedures, and should not be used too often on the same individual.

Avertin should not be employed in cases of hepatic or renal disease, in patients with a subnormal metabolism, or in elderly patients who frequently have potential kidney dysfunction and whose physiological functions will not withstand further depression.

The barbiturates, which are being used more extensively, need further investigation. The possibilities of anemia, myocardial damage and circulatory depression lack clinical confirmation. This group, when used for purposes of premedication or in conjunction with other anesthetics, may be helpful in preventing shock by maintaining the blood volume and in counteracting the hemoconcentration produced by ether. The latter can also be done by morphine<sup>9</sup> and codeine.<sup>3</sup>

When procaine is used indiscriminately in the presence of known hepatic damage, it may be that failure of the liver to detoxify the drug rapidly will result in the dangerous situation of a large amount of pure procaine being present in the circulation.

A high carbohydrate, high protein and low fat diet prior to anesthesia may help protect the liver, diminish nausea and vomiting and guard heat production. It is

possible that a small or moderate dose of insulin given several hours before anesthesia may help avoid excessive glyco-genolysis. Intravenous glucose or dilute sodium bicarbonate solutions prior to anesthesia may protect the kidneys of elderly patients.

Blood counts and blood analyses done on blood that is drawn during anesthesia and the first few days thereafter must be considered carefully, because the agent used may produce many variations from the normal.

There are a tremendous number of problems to be solved. It is hoped that as much as possible will be done under clinical conditions, in the operating room, for human physiology varies greatly from animal physiology, and a sick patient undergoing operation differs in many respects from a healthy animal, the subject of a controlled laboratory experiment.

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# A SIMPLE PLASTIC PROCEDURE OF THE FINGERS FOR CONSERVING BONY TISSUE AND FORMING A SOFT TISSUE PAD

EDWIN DEJONGH, M.D.  
DETROIT, MICHIGAN

**T**HIS procedure is to move a section of palmar surface skin to the amputated end of the finger. It has been sug-

axis of the finger, the operation has a good chance for success.

## PROCEDURE

On admission to the plant hospital the base of the finger is cleansed with benzine, green soap, alcohol and mercresin, care being taken not to get any of these into the open wound. Then 1 per cent novocaine is injected at the base of the finger, about 2 to  $2\frac{1}{2}$  cc. in each side, using care to get enough near the dorsal aspect of the finger. Rarely is more than a total of 5 cc. required.

Following this the lesion is scrubbed with green soap as is the remainder of the finger. This is followed by alcohol and mercresin after which the arm, hand and finger are draped. The wound is débrided.

The end of the remaining part of the distal phalanx is trimmed and the edges rounded and smoothed. Occasionally, the palmar edge may have to be trimmed back further than the extensor edge. This, of course, is determined by the débridement necessary. In some cases a small section of remaining distal phalanx may have to be removed.

Next a transverse incision is made on the palmar surface about  $\frac{3}{16}$  to  $\frac{1}{4}$  inch, (6 to 7 mm.), proximal and parallel to the edge of the amputation. The incision is extended from the midlateral point on one side to the same point on the other side. (Fig. 1.) The depth of the incision is not difficult to determine. It is carried down through the layers of the skin and just into the areolar tissue. A transverse section or strip of skin is free to be moved over the end though it is still attached on both its lateral ends. Under-cutting is not necessary.

All that now remains to be done is to move the section distalward and dorsally so it covers the end of the finger. This is

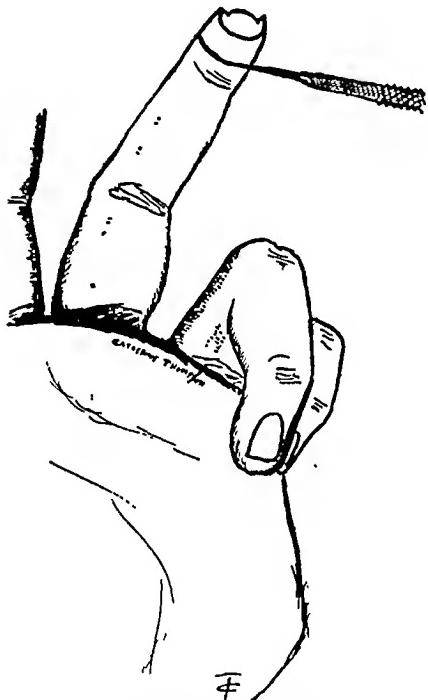


FIG. 1. Drawing illustrates line of incision forming palmar skin section.

gested that this method has appeared in the literature. The writer has been unable to find it.

In America's large industrial plants, amputation is approaching a rarity. In the smaller jobbing shops, where safety departments are less efficient, this injury is still sadly common.

The writer has had rather discouraging results with the free graft in industry. Needless to say, all digit amputations will not submit to this plastic operation. Generally speaking, an amputation through a nail, if the proximal part of the nail or its bed, remains and if the transverse line of amputation is not too oblique with the long

easily done with three, rarely more, linen sutures. The sutures are passed through the nail or its bed, and through the skin section

the tip of the finger. The pad was not as thick as usual due to lack of depth of the transverse palmar surface incision. However, it did not



FIG. 2.

FIG. 2. Left second finger of Mr. T. M. on August 25, 1941, about five minutes after traumatic amputation.

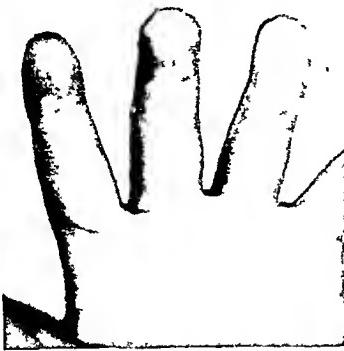


FIG. 3.

FIG. 3. Left second finger of Mr. T. M. on September 26. Note difficulty in determining scar left by moving skin section.

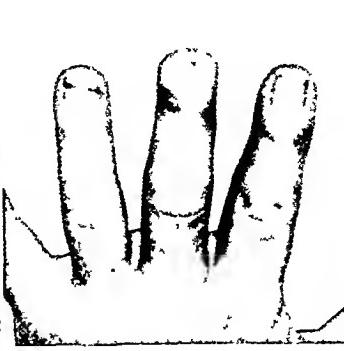


FIG. 4.

FIG. 4. Left second finger of Mr. T. M. on September 26. Note small lateral distal fragment of old nail remaining.

near the distal edge and drawn up tight under the nail or to the bed. The denuded area just proximal to the proximal edge of the skin section granulates in well and rapidly. The small scar formed, though it is on the flexor surface, is not tender and has caused no inconvenience. A vaseline gauze dressing covers the entire finger. The first dressing is done in five days and the sutures are removed about the eighth or ninth day. If removed too soon, the skin section will move toward its original position. The nail usually sloughs and a new one forms. The new nail will be shorter than its fellow and predecessor but will bear a proportional length to its finger.

The average healing time is twenty to twenty-five days with the disability depending on the patient and the ability of the department to place him for the first four to six postoperative days.

One possible failure out of twenty eight cases was noted:

J. W., a nineteen-year old female, factory worker, was operated upon in the manner described. However, in addition, a free split thickness graft was taken from the thigh and sutured on the denuded area. The graft did not take. The donor area healed as usual and required only sterile vaseline gauze dressings. After the graft sloughed the denuded area healed as usual. Three weeks after her discharge, she returned, complaining of pain at

appear to be unduly thin. There was no evidence of an amputation neuroma. The patient was asked to give the finger a trial for some time, perhaps a month, and return to the clinic if she still had difficulty. She has not been seen since.

The remaining twenty-seven patients healed rapidly. The final results were similar to those shown in Figures 2, 3 and 4. Patients are eager to avoid loss of appreciable finger length and loss of the nail. The cosmetic result is happily accepted.

There seems to be evidence that grafting the denuded area is of no value in improving the final result or in decreasing the healing time. The writer prefers not to graft.

The risk to the operation is no greater than that involved in any nerve blocking procedure and the same precautions should be observed. In case of a failure the finger can be amputated and closed with a palmar flap.

#### CONCLUSIONS

A bone conserving plastic procedure is presented which is simple and requires no special skill or instruments.

Disability is not long.

There is little, if any, risk; and the final result is a good finger functionally and cosmetically.

# Case Reports

## GASTRECTOMY FOR CARCINOMA\*

### CASE REPORT OF OLDEST PATIENT TO SURVIVE

M. G. GILLESPIE, M.D.

Chief of Surgery, St. Luke's Hospital

DULUTH, MINNESOTA

TOTAL gastrectomy is becoming a more frequent operation. According to Finney and Rienhoff, Phineus



FIG. 1. Preoperative fluoroscopy revealing extensiveness of carcinoma.

Conner of Cincinnati performed the first total gastrectomy in 1884. The patient did not recover. However, in 1897, Schlatte performed the first successful total gastrectomy.

In 1929, Finney and Rienhoff collected from the literature sixty-seven cases of total gastrectomy, and Raeder reported

eighty-eight cases up to 1933. Since that time the operation of total gastrectomy has become a more frequent occurrence. The Mayo Clinic reported twenty-seven total gastrectomies between 1907 and 1938, and sixteen since 1937. Arthur W. Allen, reporting the experience at the Massachusetts General Hospital, listed fifteen cases between the years 1932 and 1938. Lahey, in 1939, reported nine cases. Besides these, a number of single case reports have been published and it is known that other small groups of cases have not as yet been reported in the literature.

According to Walters, the indications for total gastrectomy for carcinoma are three: (1) The lesion should be confined entirely to the stomach without evidence of metastases. (2) The entire stomach and lower end of the esophagus should be sufficiently mobile to enable the surgeon to remove the stomach and to make the esophagojejunal anastomosis without too much difficulty. (3) The general condition of the patient should be good, so that the risk assumed is not too great.

The mortality rate, as might be expected, is high. Finney and Rienhoff reported in the collected group of sixty-seven cases a mortality rate of 53.8 per cent. Allen, in the group of fifteen cases from the Massachusetts General Hospital, reported 7 deaths. Lahey stated that in the nine cases of total gastrectomy, there were five surgically

\* From the Department of Surgery, The Duluth Clinic, Duluth, Minnesota. Read before St. Luke's Hospital Staff Meeting, Duluth, October 16, 1941.

successful. According to Donald, in the Mayo Clinic series of twenty-seven cases between 1907 and 1938, there were only



FIG. 2. Gross specimen removed at operation.

nine survivals, or a mortality rate of  $66\frac{2}{3}$  per cent. However, in the sixteen total gastrectomies since 1937, the mortality rate decreased to 31 per cent.

The cause of death, according to Finney and Rienhoff, as one might expect, was peritonitis in 58 per cent, shock in 22 per cent, and miscellaneous causes in 20 per cent.

According to Waugh and Giffin in the *Proceedings of the Mayo Clinic* for June 4, 1941, a patient seventy-two years old, upon whom they had performed a total gastrectomy, represented the oldest person to undergo total gastrectomy successfully as far as they could ascertain from the literature.

I wish to present the following case of a man, age seventy-nine, as the oldest individual to undergo a successful gastrectomy for carcinoma.

#### CASE REPORT

W. S., age seventy-nine, consulted Dr. P. G. Boman, August 25, 1941, because of epigastric



FIG. 3. Mr. W. S., age seventy-nine, seven weeks postoperatively.

pain and distress. This distress dated back three months. The pain was constant and dull in character. He had a poor appetite and had lost fifteen pounds in weight. There was also an associated weakness, and constipation.

The patient had first been seen in the Clinic in 1917, at the age of fifty-five. He then gave a history that for twenty-five years he had had stomach trouble. He was examined by Dr. T. R. Martin and found to have an achlorhydria. Stomach fluoroscopy was negative. He was treated with dilute hydrochloric acid.

In 1923, a bilateral herniotomy was performed by Dr. Braden. Following this he had a cystitis and prostatitis, and was under the care of Dr. Nicholson.

In 1927, he consulted Dr. P. G. Boman, because of stomach distress, and again it was found that he had an absence of free hydrochloric acid. A stomach fluoroscopy was negative. He was treated with dilute hydrochloric acid.

In 1937, he was treated for frequency of urination by Dr. Nicholson.

In 1938, he consulted Dr. Boman and it was



FIG. 4. X-ray view of the esophagojejunal anastomosis twenty-seven days postoperatively.

found that he still had an absence of free hydrochloric acid. The stomach fluoroscopy, as before, was found to be negative. Treatment with hydrochloric acid was resumed.

In 1941, he was treated for a prostatitis by Dr. Nicholson.

Family and marital histories were irrelevant.

Examination showed this elderly man to be rather thin, weighing 120½ pounds. He showed evidences of weight loss. Despite this, he was quite well preserved for his years. There was some evidence of chronic emphysema. His blood pressure was 110/80. The heart and lungs were normal for his age.

Abdominal examination revealed a mass on fluoroscopy associated with the stomach (Fig. 1), which Dr. Boman believed to be an inoperable carcinoma of the stomach. Test meal revealed an absence of free hydrochloric acid and there was three plus occult blood present.

Examination of the blood showed the hemoglobin to be 12.5 Gm. or 85 per cent, the red blood count 4,510,000. The urine was negative for albumin and sugar.

The patient was told that he had an extensive carcinoma of the stomach which probably could

not be removed. However, he and his family elected to have an exploration, and therefore he entered the hospital, September 1, 1941. September 3 he was explored.

Anesthesia was accomplished with ethylene and ether vapor. It was found that there was a diffuse carcinomatous involvement of the stomach extending from the pylorus almost to the esophagus. However, the stomach was not attached and there were no evidences of peritoneal or liver metastases. There were, however, a few enlarged glands in the gastrocolic and gastrohepatic ligaments. It was decided to attempt a total gastrectomy. The gastrocolic omentum was first divided along the greater curvature. The duodenohepatic ligament was then divided, and the duodenum cut across just distal to the pylorus. The duodenum was inverted. The attachments to the spleen were divided, which allowed for greater mobility. The right gastric artery was then divided and ligated. In this way, we were able to mobilize the cardia and the esophagus. A loop of the jejunum was brought up through the mesocolon, and an anastomosis was made with a layer of interrupted silk No. 1 sutures and two rows of No. 0 chromic catgut. The suture line was reinforced with omentum. A jeunojejunostomy was then performed. A gastro-enterostomy tube which had previously been inserted was then brought down through the anastomosis well along into the distal loop of the jejunum. Finally, the mesocolon was sutured about the loop of the jejunum. A penrose drain was inserted below the inferior surface of the liver. Two Gm. of sulfanilamide powder were left in the operative area and another 2 Gm. were placed in the wound during its closure. He was given 500 cc. of 5 per cent glucose and 1,000 cc. of citrated blood during the course of the operation. The operative procedure took almost three hours. At the close, his systolic blood pressure was 120 and the diastolic pressure 70.

Dr. A. H. Wells\* submitted the following report on the gross specimen (Fig. 2):

"Specimen consists of a large mass of stomach, including about 2 cm. of the duodenum. When spread out it measures 20 cm. long and 12 cm. wide. The entire pyloric end, including

\* Pathologist, St. Luke's Hospital, Duluth, Minnesota.

the pyloric valve, over an area measures about 13 cm. in length is hard, diffusely and severely thickened, but apparently not extending into the duodenum. The mucosal surface over this area is fixed and gray. The submucosa and muscularis are uniformly indurated, gray, firm and thickened, averaging 1½ cm. in breadth. The serosa is likewise unusually gray and fixed to deeper tissues. At the fundal end there is apparently 5 cm. of normal appearing mucosa. There is no ulceration of the involved mucosal surface.

"Microscopic: There is a wild, very diffuse invasion throughout the various layers of the gastric wall by highly anaplastic and very small epithelial cells. Occasionally these cells form definite glandular structures.

"Diagnosis: Scirrhous carcinoma of stomach (N<sub>5</sub>-d<sub>2</sub>-ca. stomach)."

Feedings through the gastro-enterostomy tube were begun on the second day. For two or three days there was rather profuse drainage through and about the penrose drain, but this gradually decreased, and his wound healed without infection. The gastro-enterostomy tube was removed on the fifth postoperative day, and thereafter frequent small, oral feedings were given. He was allowed out of bed on the

ninth postoperative day and left the hospital on the sixteenth postoperative day.

#### SUMMARY

A patient (age seventy-nine) is presented who was operated upon for carcinoma of the stomach. Total gastrectomy was performed. The patient made an uneventful convalescence and I believe is the oldest patient to survive this procedure. At the time of this writing, almost three months following operation, his recovery has continued to run a smooth course.

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# MALIGNANT MELANOMA OF THE RECTUM\*

## REPORT OF A CASE

CHARLES GOLDMAN, M.D.

AND

GREGORY L. ROBILLARD, M.D.

Assistant Surgeon, Cumberland Hospital

Attending Surgeon, Norwegian Hospital

BROOKLYN, NEW YORK

THE exact origin and the significance of melanin in malignant melanomas is a matter of controversy. The uncertainty of its origin is shown by the presence of melanin in both carcinomatous and sarcomatous growths. Although melanin occurs normally in the choroid of the eye, in the skin and in the hair, and is found in fairly large amounts in certain new growths and in melanotic tumors, it is extremely difficult to obtain it in any quantity and in a purified form. Melanin is difficult to isolate since it does not crystalize and it is insoluble in fluids which do not change its composition. Melanin is soluble in a strong alkali or acid, which, however, changes its composition. This makes it extremely difficult to learn its exact chemical composition and presents a fundamental difficulty in studying melanin in normal and pathologic cells. An added difficulty is the presence of melanin in foods of plant and animal origin and its normal formation within the body. We often find melanin in the mucosa of the appendix, in the colon in chronically constipated individuals, and in the epithelium of the collecting tubules of the kidneys in adults.

It is believed that melanins are a group of nitrogenous compounds closely related to the proteins. Some believe that melanin found in tumors is purely of endogenous source, originating either from a special pigment cell, or from cells which have taken on the function of pigment formation. Dawson studied a number of benign and malignant melanomas, none of which occurred in the anus. "The term melanoma," he says, "emphasizes the specific character of the tumor cell, which contains

a variable amount of an iron-free pigment, melanin. Color or pigment production in the animal kingdom, especially in the highly pigmented vertebrates, the frogs and reptiles, has long been held to belong essentially to a specific cell, the 'chromatophore,' and the claim of the exclusive relation of this cell to pigment production is only emphasized in the admission (a) that the overflow from the chromatophore may be transported to epithelial cells of the epidermis, and (b) the deposit of this excessive pigment from the mesoblastic chromatophore, in certain cells of the foetal epidermis may excite these cells to proliferate and cause them to assume the function of pigment production. The pigment cell, on the other hand, is held by others to have arisen from the ordinary connective tissue cell of the corium, or to be of endothelial origin, or again exclusively of epidermal origin, with the further contention that the connective tissue cells merely carry off the surplus in the lymph paths."

We may or may not admit the specific character of the cells which form the melanin pigment, but we all recognize the great variation in the histologic makeup of tumors containing the pigment. Even though we admit the source we still do not know the significance of the presence of the pigment in malignant tumors.

Chalier and Bonnet have analyzed sixty-four cases of melanomas of the intestinal tract and found that 2 or 3 per cent of all melanomas occur in this region, and that most of these are found in the rectum. They see a resemblance of these tumors to epidermoid carcinoma, and believe that these tumors are derived from the anal epi-

\* Read before the American Proctologic Society, June, 1941, Cleveland, Ohio.

dermis and infiltrate beneath the mucosa. Ewing in his book on "Neoplastic Tumors" discusses and summarizes the theoretic origin of melanomas in a masterly manner.

from this stem and was in the rectum. It was nodular and hard. On the right side of the mass was a similar one, about the size of a small nut, arising from a small band above the anus.



FIG. 1. Study of section of mass removed May 15, 1939. Stroma is the site of dense neoplastic infiltrative process consisting of single cells, groups of cells and irregular acini (lower power).

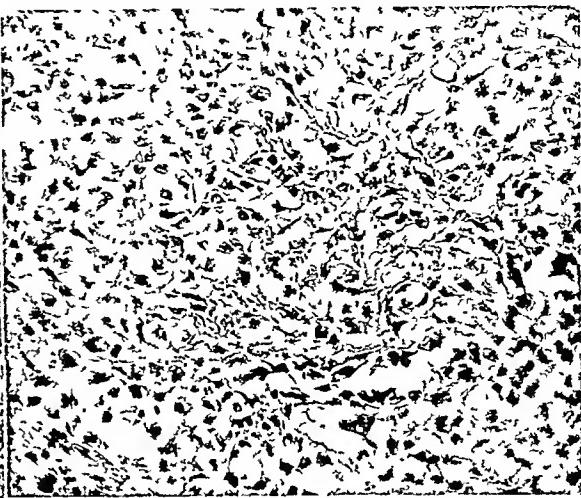


FIG. 2. Study of section of mass removed May 15, 1939. The cells show a marked variability in size and shape of nuclei; innumerable mitotic figures are present (high power). Diagnosis: anaplastic carcinoma.

We present a case of malignant melanoma of the rectum with four photographs. The patient has been followed from May 14, 1939 to the time of her death, March 9, 1941.

#### CASE REPORT

S. P., a female, aged forty-nine, was admitted May 14, 1939 to Coney Island Hospital, and discharged May 28, 1939. She had a protruding mass from the rectum.

During the past two years the patient had been troubled with a protruding mass from her rectum following each bowel movement. At first the mass was small and reduced itself spontaneously. During the past eight months it had become larger and more difficult to reduce. Patient moved her bowels six to seven times daily, a small amount at each movement. There was no watery diarrhea. The stools were normal in contour and brown in color. Tenesmus was present at each bowel movement and there was bleeding at times with stool.

On rectal inspection there was slight eversion of the anal mucosa on straining. One small hemorrhoid was seen. One could feel a lemon-size, nodular, pedunculated mass, whose stem was thin and close to the anus. The mass arose

Impression: Anal polyp-external hemorrhoid. The patient was operated upon May 15, 1939.

The specimen consisted of two irregular masses, the larger measuring 3 by 2 by 2 cm., pinkish in color and nodular in outline. On section the mass was homogenously grayish-white.

Microscopically, the sections were covered in one area with stratified squamous epithelium, showing transition to columnar epithelium. (Figs. 1 and 2.) The entire stroma was the site of a dense, neoplastic infiltrative process consisting of single cells, groups of cells and irregular acini. The cells showed a marked variability in size and shape of the nuclei. Innumerable mitotic figures were present. The entire process was one of immaturity.

Diagnosis: Anaplastic carcinoma of the rectum.

The patient refused radical surgery and was referred on May 28, 1939 to the Brooklyn Cancer Institute, at the Kings County Hospital, Brooklyn, New York.

At the Brooklyn Cancer Institute, where we saw the patient the history was as follows:

The patient, S. P., a female, aged forty-nine, was admitted June 6, 1939 and discharged July 7, 1939 with a complaint of rectal tenesmus.

On palpation a small, pea-sized nodule was felt just above the sphincter on the posterior wall. This appeared to be an inflammatory

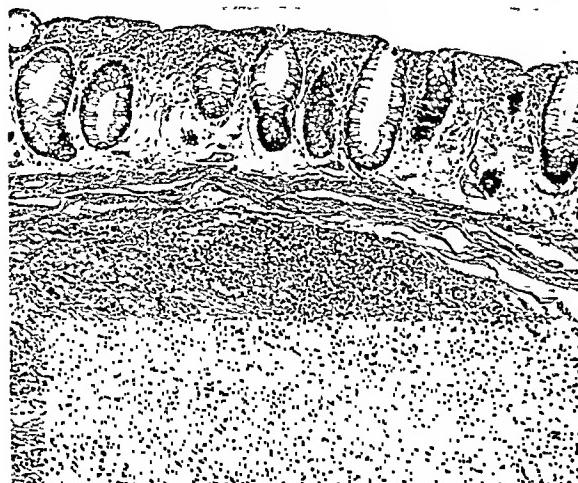


FIG. 3. Study of section of mass removed September 20, 1939. Rectal mucosa is intact. In the submucosa are seen multiple, large, fairly discrete masses of atypical cells; there is occasional pseudogland formation (low power).

thickening. Proctoscopic examination revealed what appeared to be an inflammatory mass on the posterior wall about 1 cm. in diameter, with a dark bluish mass just above. The patient, however, refused operation and signed her release July 7, 1939. During the interval the patient received deep x-ray therapy. The patient was admitted a second time on September 20, 1939 complaining of severe rectal tenesmus. Examination at this time showed that the mass was now about 1½ cm. in diameter and the bluish mass just above had increased in size. The patient was taken to the operating room for removal of the growth for biopsy and the insertion of radon seeds. The pathologic report was as follows:

The rectal mucosa was intact, one portion undergoing compression atrophy, due to the presence in the submucosa of multiple, large, fairly discrete masses of atypical cells. (Figs. 3 and 4.) The majority of these were in no definite arrangement. An occasional group tended to form a pseudogland. The individual cells were large, with poorly defined cell boundaries, a pale pink or foamy cytoplasm and nuclei which vary considerably in appearance. The majority were vesicular, round or ovoid, with small basophile nuclei. Others were hyperchromatic and irregular, with occasional regular mitotic figures. In some areas both in

the stroma and within the tumor cells were collections of granular brown pigment which did not take the stain for iron. There was a

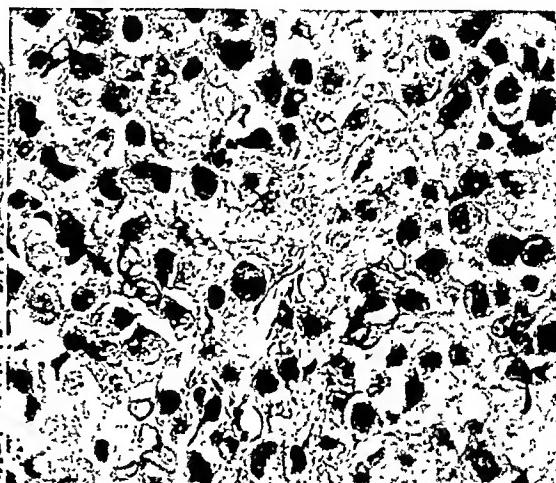


FIG. 4. Study of section of mass removed September 20, 1939. The individual cells are large, with poorly defined boundaries. The majority are vesicular, round or ovoid, with basophilic nuclei. Others show hyperchromicity, anaplasia and mitosis. In some areas, collections of granular, brown pigment which do not take the stain for iron are seen located in either the stroma or tumor cells. Fibrous reaction and lymphocytic infiltration are slight (high power). Diagnosis: malignant melanoma.

little fibrous reaction and a scant infiltrate of lymphocytes. Diagnosis: Malignant melanoma.

At the patient's insistence and her refusal of further treatment she was discharged on September 25, 1939, and referred to the outpatient department. On October 5, 1939 there were numerous pigmented spots on the left arm, left side of the neck and on the left wrist. The patient refused all further treatment.

The patient got along fairly well at home for almost one year, when she began to complain of weakness in her legs and for several weeks inability to walk. She was readmitted to the hospital for the third time on November 14, 1940, when examination showed for the first time enlargement of the inguinal lymph-nodes. One of the lymph-nodes was removed for biopsy with the following report:

Small areas of lymphoid tissue still remained. The remainder of the node was completely replaced by tremendous sheets of atypical cells, closely crowded, but tending to have an alveolar arrangement. The individual cells were large, many were round, or polyhedral in outline, with distinct cell boundaries; others appeared inter-

connected by fine processes. The cytoplasm was pale pink, the nuclei varied considerably in size, shape and staining capacity. They were either vesicular or hyperchromatic and irregular, and had occasional multinucleated cells. There were scattered regular mitotic figures. Fibrous reaction was minimal. No pigment was present.

Diagnosis: Metastatic melanoma (rectal origin).

X-ray examination showed the following: On November 25, 1940 there was no evidence of bone metastasis to the spine. Chest plate showed a supraventricular shadow, from which a soft tissue mass bulged into the left lung field for about one inch. The mass had a well-defined, irregular wavy outline. On December 2, 1940, the right foot showed rarefying metastasis of plum-pit size within the base of the fifth metatarsal and the third metatarsal bones. A pathologic fracture was noted in the third metatarsal, and there was a rarefying metastasis in the posterior aspect of the fibula two inches above the lower end. On December 3, 1940 a rarefying metastasis in the left ring finger, right metacarpal bone, left foot third metatarsal and metastasis in both femurs was noted. On December 11, 1940, numerous rarefying metastasis about 1 cm. in diameter was seen in the lateral skull. On January 31, 1941, a pathologic fracture of the right femur occurred and involvement of the right half of the pelvis was noted.

The patient expired in the hospital on March 9, 1941. We are embarrassed in not having the autopsy findings, but at the time the patient expired four of the resident surgeons left the hospital to enter the Army. We were not notified that the patient had expired until

the following day, when we found that the body had been removed without a request for an autopsy, which we are certain would have been granted.

#### SUMMARY

1. The origin and significance of melanin in malignant tumors is reviewed.
2. Melanomas of the intestinal tract constitute 2 to 3 per cent of all melanomas and are most frequently found in the rectum.
3. A case of malignant melanoma of the rectum is reported.

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# TUBERCULOSIS OF THE THYROID GLAND WITH HYPERTHYROIDISM\*

## CASE REPORT

HARRY N. COMANDO, M.D.  
Attending Surgeon, Newark City Hospital  
NEWARK, NEW JERSEY

**T**UBERCULOSIS of the thyroid gland is rarely evident clinically. There are two types of the surgical forms of this disease reported: One assumes a clinically symptomless course or is associated with hyperthyroidism; the other consists of the cases of chronic tuberculosis of the thyroid gland in which great numbers of isolated nodules increase in extent, or the gland enlarges through caseation and abscess formation. Under the latter circumstances, symptoms supervene which differ from the usual goiter symptoms and are variably interpreted. The latter frequently suggest malignancy, Riedel's struma, etc. Rarely are they diagnosed as tuberculosis.

The case about to be reported, belongs to the first group, that is, tuberculosis of the thyroid gland associated with Basedow's disease. This clinical entity has been previously described both clinically and histologically, and it is a generally accepted fact that tuberculosis is a cause of Basedow's disease, notwithstanding the claims of several investigators to the contrary.

The case about to be reported was free of any tuberculous manifestations and the course was so unusual and different, that a detailed review of the literature would be out of place here.

### CASE REPORT

The patient, Mrs. D. M., was first seen June 14, 1938. Her present illness began four months previously with loss of appetite, vomiting and occasional diarrhea. The patient felt weak and tachycardia was present on slightest

exertion or excitement. She slept well and had lost thirty-five pounds in five months.

Her pulse rate during this examination was 140, basal metabolic rate, plus 40; there was no dyspnea, cough, or melena.

The patient was put on Lugol's solution m-x and phenobarbital gr. ss three times a day and was told to rest. Later, June 26, 1938, she was admitted to the Beth Israel Hospital. The history given by the patient at that time was essentially the same, except that her pulse had slowed down considerably. The physical examination showed a fairly well nourished, white female, forty-three years old. She was sixty-one inches tall and weighed 129 pounds.

There was a slight exophthalmos, no lid lag, the pupils were normal, and the throat was not injected. There were no palpable lymph glands. There was a suprasternal mass in the midline and right side which moved up and down on swallowing.

The chest and lungs were negative to percussion and auscultation. The heart sounds were of good quality, sharp and accentuated. Blood pressure was 120/80. The abdomen was negative for any pathological finding. There was a slight tremor of the right upper extremity. The basal metabolic rate taken June 29, 1938, was plus 28. X-ray picture of the neck and chest was entirely negative.

Blood Count: Red cells—4,300,000  
White cells—7,700  
Polynuclears—76%  
Hemoglobin—86%

Blood Chemistry: Wassermann—negative;  
Kline—negative.

Urea nitrogen, 28.  
Cholesterol, 375.  
Cholesterol esters, 150.  
Sugar, 88.

\* From the Surgical Service, Newark Beth Israel Hospital.

A blood iodine determination was not done. The vocal cords were normal.

The patient was sent to bed and Lugol's solution and phenobarbital were continued. She continued to respond well, and gained five pounds in eight days. The pulse showed a steady rate between 80 to 90.

A subtotal thyroidectomy was performed on July 5, 1938. A bilateral multiple adenoma containing numerous white nodules, some calcified, was removed. The pathological report of the specimen was as follows:

*Gross Examination.* The specimen consisted of two lobes of thyroid tissue together with the isthmus. They measured 4 by 3 by 1½ cm., 4 by 2½ by 2 cm. and 2 by 1 by 1 cm. The surface of each portion was smooth and intact, except at the point of resection. The tissue was moderately firm in consistency and, on section, was composed of brownish-red and reddish, fleshy-appearing tissue. In addition, there were numerous well defined cystic structures, varying from 1 to 1½ cm. in diameter. These were, for the most part, surrounded by a thick wall of greyish and greyish-yellow fibrous-appearing tissue and were filled with reddish, yellowish-red and brownish, soft, almost friable tissue. Still other cystic structures which were present were smaller, being from 2 to 3 or 4 mm. in diameter, and were filled with a gelatinous greyish material.

*Microscopic Examination.* The thyroid follicles varied greatly in size. The majority were lined by cuboidal epithelium which enclosed the homogeneous eosinophilic colloid. There were occasional greatly enlarged follicles, lined by a thick wall of fibrous tissue and an inner lining of flat cuboidal epithelium filled with colloid and red blood cells. Distributed irregularly throughout the section were thick cords and thinner strands of fibrous tissue distinctly separating follicles from each other in some areas and encapsulating groups of follicles in others. Collections of round cells were found within the fibrous strands, as well as areas of hyalinization and calcification. An occasional granulomatous area was found consisting of necrotic débris in the center, surrounded by epithelioid cells, giant cells and round cells, the latter being more numerous at the periphery areas. No acid-fast bacilli were found in the granulomatous nodules.

The postoperative course was uneventful except for a moderate degree of hoarseness.

Laryngoscopic examination showed both vocal cords in central position and fixed. It was feared that this might be a permanent condition due to possible nerve injury, however, the right cord recovered about five days after the operation. Examination on October 12, 1938, in the out-patient clinic showed complete recovery.

The patient was allowed out of bed on July 12, (eight days postoperatively), but as a precautionary measure was not allowed to leave the hospital until July 24, (twenty days postoperatively). The wound was entirely healed at this time and the patient gained 8 pounds in weight.

On August 28, 1938, she presented herself to Dr. Rados, complaining of pain and redness of her right eye. An ophthalmological report follows:

The patient was first seen on August 28, 1938. She complained of painfulness and redness of her right eye for the past three weeks. One month previously, thyroid operation was performed by Dr. Comando.

Vision in the right eye was 15/20, in the left eye, 15/20. The right eye showed marked ciliary congestion, numerous small white deposits on the lower part of the Descemet membrane. The right pupil was much smaller than the left and the fundus was not clearly visible; the left fundus was normal.

*Diagnosis:* Acute iridocyclitis of the right eye.

Wassermann and Kline tests were negative; the Mantoux test was strongly positive after twenty-four hours.

On September 9, the patient showed marked deep infiltration of the posterior layers of the cornea. The infiltration was spotty in type, the iris hyperemic; at the pupillary margin, at 12 o'clock, 6 o'clock and 7 o'clock, small grayish vascularized nodules were present. Ciliary congestion increased and the eye was very painful.

*Diagnosis:* Keratoiritis and tuberculum of the iris in the right eye.

Tuberculin treatment was instituted and has worked very satisfactorily.

On January 19, 1939, the ciliary congestion had cleared up and the eye was white and painless. There were numerous, small, deep-seated corneal opacities corresponding to the previous sites of the infiltrates, the tuberculum of the

iris had gradually been absorbed, the pupil was dilated to maximum and there were no inflammatory symptoms in the iris and the ciliary body.

The clinical findings and the prompt response to the administration of tuberculin indicate the tuberculous nature of the lesion.

#### SUMMARY

The unusual features of this case are:

1. A bilateral nodular toxic goiter with areas of calcification, etc., was present.
2. No primary tuberculous lesion elsewhere in the body was demonstrated.
3. Tuberculosis of the eye followed about five weeks after the thyroidectomy. This was undoubtedly metastatic and was probably brought about by the operation.
4. There was complete recovery of the eye following treatment with old tuberculin and the patient was in perfect health six months after the operation. The eye healed completely, 35 pounds in weight were gained, and the basal metabolic rate was plus 4.

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# ANEURYSM OF THE HEPATIC ARTERY\*

H. REMBERT MALLOY, M.D.

Assistant in Pathology, Howard University

AND

ROBERT S. JASON, M.D.

Professor of Pathology, Howard University

WASHINGTON, D. C.

THE object of this paper is to report a case of aneurysm of the hepatic artery and to discuss the subject in the light of the information available.

## CASE REPORT

A housewife, fifty-two years old, was brought to Freedmen's Hospital on December 8, 1940, in severe collapse. Her daughter related that about one month earlier the patient had complained of severe abdominal pain, following a heavy meal and that for a few days thereafter tarry stools were passed. Four days prior to admission she suffered a second attack, following a heavy meal, which was characterized by persistent epigastric pain, hematemesis, later melena and eventually "shock."

The patient was of normal development, well nourished and presented the following salient findings: restlessness in spite of evidences of severe collapse; blood pressure 60/40; icteric sclera; pale mucous membranes; natural but rapid and somewhat faint heart sounds; natural lung fields; soft abdomen, though tender above the umbilicus; liver, spleen or abnormal masses not palpable.

The erythrocyte count was 1,940,000; hemoglobin 42 per cent; leucocyte count 16,780. The urine was not examined: the patient did not void while in the hospital and she was not catheterized.

Because of the history and clinical evidences of hemorrhage, immediately after admission the patient was given by vein 300 cc. of whole blood followed by 3,500 cc. of 5 per cent glucose in normal salt solution. Shortly thereafter, the patient had a severe hematemesis amounting to about 450 cc. In spite of the administration of additional fluids, the patient failed to improve and expired at 11:00 A.M., December 9, 1940, slightly over fourteen hours after admission.

The significant external findings two hours after death were pallor and unclotted blood in the oral cavity and rectum. There was no free fluid in the abdominal cavity, but the stomach,

cecum and ascending colon were distended with clotted and unclotted blood, amounting to 1,365 cc. in the stomach and 950 cc. in the proximal colon. In the duodenum, 3.5 cm. from the pyloric sphincter, there was a bleeding ulcer 5 by 7 mm. in size and within 1.5 cm. distally there were two nonbleeding ulcers 3 and 4 mm. in diameter. These ulcers occupied a dark purple and softened oval area 3 by 5 cm. in diameter, located about the center of a swelling 4.5 by 9 cm. in size, involving most of the posterior wall of the first and second parts of the duodenum. These lesions were in relation to a large, partially hemorrhagic and firm mass, with foci of softening, found behind the duodenum and extending in the gastrohepatic ligament from the pancreas to the hilum of the liver. The liver was normal, but the gallbladder was compressed slightly on the medial side; the extrahepatic bile ducts and the portal vein were displaced backward and slightly to the right and were compressed; the foramen of Winslow was obliterated; the head of the pancreas was the seat of hemorrhage and the duodenal wall was necrotic in relation to parts of the hematoma. This mass had resulted from an aneurysmal dilatation of the hepatic artery 2 cm. from its origin and a perforation in relation to the head of the pancreas and duodenum, producing a hematoma. The preserved parts of the intima within the aneurysm showed wrinkling together with calcification in areas of atherosclerosis. The walls had a lobulated contour; the lumen was filled with a laminated thrombus. (Fig. 1.) The left branch of the hepatic artery was found coursing upward to the liver from the superior surface of the aneurysm at a point about 4.5 cm. from the latter's proximal end. The right branch was traced from the liver to the superior surface of the aneurysm, about 1.5 cm. to the right of the origin of the left branch, but no opening into the aneurysm was found at this site.

The circulatory system showed in addition to the lesions of the hepatic artery, moderate hypertrophy of the left ventricle of the heart

\* From the Department of Pathology, College of Medicine, Howard University, Washington, D. C.

and mild atherosclerosis of the aorta and its main branches. The respiratory system revealed slight aspiration of blood into the larger



FIG. 1. Aneurysm of the hepatic artery. Above, the duodenum overlies the aneurysmal mass. Below, the duodenum is displaced to the right and the hepatic artery is indicated by the double thread in the upper part of the photograph.

bronchi. The other gross findings were not significant.

Microscopically, there were no recognizable syphilitic lesions of the aorta. The intima showed early atherosclerosis and the media widespread areas of degeneration, showing basophilic staining. A longitudinal section extending from the hepatic artery into the aneurysmal sac revealed a nearly normal arterial wall, thickened by fibrosis of the adventitia and slight intimal atherosclerosis, which changed gradually, showing irregularly progressive thickening of the intima by atherosclerosis with focal calcification over a thinning media and a progressively thicker adventitia. (Fig. 2.) Similar but more severe intimal changes were found in other sections of the aneurysm where the media was replaced in large measure by fibrous tissue in the form of scars which united in places the fibrous tissue of the intima with the thickened adventitia. Overlying the intima were thrombi, showing

layers of varying ages. The thickened adventitia was the seat of leucocytic infiltration, consisting of lymphocytes, plasma cells and



FIG. 2. Longitudinal section of the proximal part of the aneurysm.

monocytes, aggregated particularly about blood vessels but the latter did not show obliterative intimal proliferation. (Fig. 3.) Focal collections of similar cells with small capillaries forming granulation tissue were found focally where the media was severely compromised and in places this type of tissue with some collagenous deposits was the entire aneurysmal wall. Toward the duodenum the vascularized scar tissue which constituted the aneurysmal sac gave way so that blood clots were adjacent to the muscle coats. This rupture appeared to have been recent, for well preserved erythrocytes were identified in the clot and there was very little leucocytic infiltration of the duodenal wall at this site.

In the liver there was a widespread and severe microphage infiltration of the sinusoids with degeneration of the cord cells and occasional foci of necrosis. In the kidneys there was slight arteriosclerosis with an occasional cortical scar bearing hyalinized glomeruli. In the other organs the changes were not significant aside from slight edema of the lungs.

#### DISCUSSION

**Incidence.** Aneurysms of the hepatic artery are among the rarer types of vascular lesions. The latest comprehensive report made in English appeared in 1923 when Friedenwald and Tennebaum<sup>3</sup> added a case to the sixty-four they had been able to find recorded up to that time. We have found nineteen additional reports, which with our own, brings to eighty-five the number of cases now on record.<sup>1-2,4-20</sup>

**Sex.** The condition is found in a 3:1 ratio in males and females, for of the eighty-

two cases in which sex was recorded, sixty-two were males and twenty females.

**Age.** The age distribution is wide: the youngest case being a boy ten years old and the oldest a man of eighty-three years. The average for the entire group was thirty-eight years; for males thirty-six years and for females forty-two years.

TABLE I

ETIOLOGY OF ANEURYSMS OF THE HEPATIC ARTERY  
Infections.....

With Inflammation at the Aneurysmal Site.....	16
Syphilis.....	7
Cholecystitis.....	4
Liver Abscess.....	2
Peri-arteritis.....	2
Tuberculosis.....	1
Likely to Produce Inflammation at the Aneurysmal Site.....	21
Pneumonia.....	7
Osteomyelitis.....	4
Bacterial endocarditis.....	3
Embolism—source not stated.....	2
Typhoid fever.....	2
Influenza.....	1
Phlegmon of leg.....	1
Suppurative mediastinitis.....	1
Not Likely to Produce Inflammation at the Aneurysmal Site.....	3
Pleurisy.....	1
Pulmonary tuberculosis.....	1
Type of infection not stated.....	1
Arteriosclerosis.....	15
Trauma.....	7
Cholelithiasis.....	5
Diagnosis not stated.....	17
Total.....	85

**Etiology.** The causes of the condition are varied but infectious processes appear to be the most important group, accounting for forty-one or 60 per cent of the sixty-eight cases in which the cause was given. Next in order of frequency are arteriosclerosis with fifteen cases (22 per cent) and trauma with seven cases (10 per cent). The infectious processes reported vary from those which appear to have been the causes of aneurysms to those in which this relationship appears improbable. (Table I.) It is of interest that syphilis, which is the most common cause of aneurysms of large arteries, ranks well below arteriosclerosis with only six cases in which it appeared to have been the cause and one doubtful case. Though cholelithiasis has been reported as a cause in five cases, we are of the opinion with Tenani<sup>18</sup> that the concomitant cholano-

gitis is perhaps a more important factor than the pressure afforded by the concretions. It is conceivable that in cases wherein

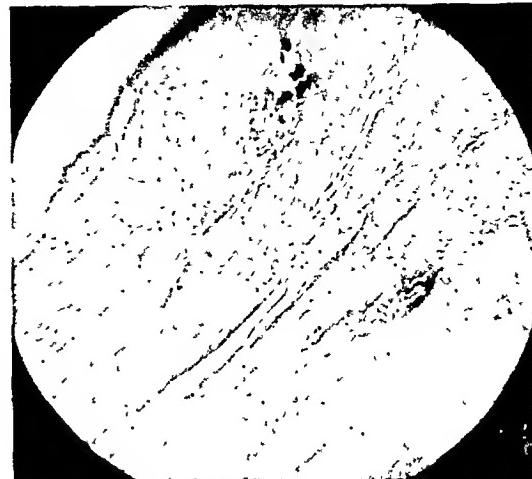


FIG. 3. Higher magnification of the part of the aneurysmal wall indicated by the India ink dot in Figure 2. The intima is thickened by atherosclerosis with a focus of calcification and is overlaid in part by a thrombus; the media shows a defect beneath the point of calcification; the adventitia is thickened by scarring, and its perivascular lymphocytic and plasma cell infiltration is not associated with obliterative endarteritis.

the lesion encroaches upon a passage of the digestive system, the intake of food and the normal processes of digestion may, as in our case, be a factor in precipitating hemorrhage.

**Pathology.** Grossly, the most important features about aneurysms of the hepatic artery are their position, number, size and relationship to adjacent structures. Based upon their position, either within or without the liver, these aneurysms have been subdivided into two groups: the intrahepatic and extrahepatic. The latter is by far the larger group for of the eighty-four case reports in which the positions of the aneurysms were recorded, sixty-one subjects had them outside of the liver; twenty had them within the liver and three subjects had both intra- and extrahepatic aneurysms. Based upon the artery of origin, the distribution was: hepatic artery—forty; right branch—twenty-six; left branch—seven; both right and left branches—one; cystic artery—three and gastroduodenal artery—one.

These aneurysms are usually single, though the following instances of multiple aneurysms have been reported: two aneurysms in each of six cases; three in three cases; four in one case; five in one case and "several" in one case.

The aneurysmal sacs vary from the size of barleycorn as found by Rolland to that of a child's head, as found by Wallmann.<sup>3</sup> The extrahepatic sacs are usually larger than the intrahepatic ones, though the largest intrahepatic aneurysm recorded, that of Pugliatti,<sup>14</sup> was about the size of a full-term fetal head.

The smaller aneurysms of the hepatic artery are usually true aneurysms, resulting from a dilatation of the vascular wall; the larger ones, however, are in part false aneurysms or hematomas, resulting from the rupture of the weakened vascular wall into the retroperitoneal tissues. Both the true and false aneurysms become adherent to surrounding structures by fibrous adhesions of varying density and may cause compression, particularly of the bile ducts. Eventually, most of the aneurysms rupture either into the abdominal cavity, which is true in most instances, or into some adjacent structure. Rupture occurred in sixty-seven of the eighty-five cases reported to date. Of this number thirty-one ruptured into the abdominal cavity; twenty-two into the extrahepatic bile ducts; seven into the duodenum; six into the gallbladder; one into the stomach and one into the portal vein. In four subjects there were double ruptures: in two rupture occurred into the duodenum and abdominal cavity; in one into the gallbladder and abdominal cavity and in one into the hepatic and common bile ducts. Of special interest are the reports of two subjects<sup>3</sup> who had exhibited clinically hemorrhage into the gastrointestinal passages though at necropsy no perforation of their intrahepatic aneurysms was found. We believe that in these cases and perhaps in others, a rupture occurred into intrahepatic bile ducts.

Microscopically, in addition to the evidences of recent and remote hemorrhage and thrombosis, there are evidences

of inflammation and less frequently of arteriosclerosis. In the vessel wall the inflammatory reaction is commonly in keeping with a traumatic or bacterial origin but only rarely syphilitic. Atherosclerotic changes with calcification, of sufficient degree to be considered of etiologic importance, are found in nearly a fourth of the cases. In all aneurysms, but particularly in the older ones, there is evidence of healing which ranges from granulation tissue growth into the sites of hemorrhage and thrombosis to dense collagenous scarring.

*Symptoms and Signs.* The symptoms and signs of aneurysms of the hepatic artery are varied, but there are three which occur with sufficient frequency to warrant considering them specially as aids in diagnosis. These are: pain, hemorrhage and jaundice. Pain is by far the most common of these, occurring in fifty-eight cases. It is usually felt in the right hypochondrium or in the epigastrium or both; it varies in intensity from a feeling of pressure to severe colicky pains; it may be intermittent or constant and its onset may be precipitated by a known factor or without apparent cause.

Next in frequency is hemorrhage which occurred in forty instances. It is usually profuse and in the form of hematemesis or melena, though occasionally it is detected merely as occult blood in the stools and in some instances repeated small hemorrhages produce secondary anemia. Whenever hemorrhage is apparent externally, the aneurysm has ruptured either directly into the digestive passages or indirectly through the biliary ducts, but cases of hemorrhage into the liver or into the abdominal cavity may not be recognized except by the signs and symptoms of internal bleeding. When pain and hemorrhage occur in the same patient, hemorrhage usually follows pain.

Jaundice is the least frequent of the three most common symptoms and signs, occurring in thirty-six cases. It is usually of the obstructive type and is caused by compression of the common duct by the aneurysmal sac or by rupture of the aneurysm into the

duct causing obstruction by a clot. In many cases the jaundice is intermittent, but it may be persistent and severe, accompanied by pruritus.

Less common symptoms are fever, noted particularly in those cases associated with infectious processes and also asthenia, headaches, constipation and ascites. A pulsating tumor with a systolic murmur and enlargement of the liver are considered by Lambert and Secretan<sup>6</sup> and by Bickhardt and Shumann<sup>3</sup> as important signs.

**Duration.** The duration of the condition from the time of onset of symptoms or signs to the diagnosis, varies from a few hours to several months, with an average of about four or five months.

**Diagnosis.** Largely because of the rarity of aneurysms of the hepatic artery, their diagnosis is seldom made, having been made before death or operation in only two cases, though there are instances wherein the diagnosis was made at operation. It would seem, however, that having the condition in mind, the diagnosis should not be difficult in a subject exhibiting epigastric or right hypochondrial pain, hemorrhage and jaundice, particularly so when the process accompanies or follows a generalized infection. If the patient should present in addition a pulsating abdominal tumor with a systolic murmur and enlargement of the liver, the diagnosis of aneurysm of the hepatic artery should be relatively easy. In arriving at a diagnosis the more common pathological processes affecting the tissues and organs of the right upper quadrant of the abdomen and lower chest must be considered and ruled out.

**Treatment.** The treatment of aneurysms of the hepatic artery, like that of aneurysms in general, is unsatisfactory. Ligation, the only form of therapy employed to date, is dangerous because it is likely to result in death from liver necrosis or insufficiency. Yet, the facts that there are recorded two instances of recovery after operation and that some cases recover spontaneously, offer the hope that if the diagnosis were made, the surgical approach, (perhaps by gradual reduction of the blood supply to

the part and the establishment of a collateral circulation) might lead to a larger per cent of cures. At present, however, the prognosis is decidedly unfavorable.

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# PERFORATED PEPTIC ULCER COMPLICATED BY ACUTE PURULENT APPENDICITIS\*

## CASE REPORT

ALEXANDER W. SANDERS, M.D.

Associate Surgeon in Gynecology, North-End Clinic  
DETROIT, MICHIGAN

THAT a patient having a peptic ulcer may also harbor chronic appendicitis is a well known fact. However, the incidence of a perforated peptic ulcer complicated by acute appendicitis is very rare. This is borne out by the fact that in the medical literature for the last fifteen years, only nine such cases have been reported. Of these, eight were found in the French, Italian, Russian and Spanish medical literature and one in the English.

In addition, a case that suggested the co-existence of the two conditions was reported in 1911 by Andre.<sup>2</sup> An appendectomy was performed on a woman presenting the signs and symptoms of acute appendicitis. During convalescence she developed a cough with purulent expectoration. Cultures of the sputum showed streptococci, staphylococci, and Koch bacilli. The patient died and the autopsy revealed a subdiaphragmatic abscess connected with a fistula to a perforated round ulcer of the pyloric portion of the duodenum. The perforation is supposed to have occurred after the appendectomy.

Another case in point that borders closely on the type of cases discussed in this paper is that reported by R. W. John.<sup>13</sup> A boy six years old was operated upon for acute suppurative appendicitis. Six days after the operation he died of hemorrhage. At autopsy "a perforating ulcer was found on the posterior wall of the duodenum, which penetrated the entire gut and eroded the gastro-duodenal artery and caused the fatal hemorrhage."

## CASE REPORT

C. T., age twenty-three, a male factory employee, was well when he went to bed at 1 A.M. on August 31, 1941. Before retiring he drank a bottle of carbonated water. At 5 A.M. a sudden stabbing pain in the abdomen awakened him. He vomited shortly afterward. The pain was continuous and was accompanied by pain in the left shoulder. One and one-half hours later I found him sitting up in bed in a doubled-up position with his hands over the abdomen pressing against the epigastrium and umbilical region.

Four years ago he had severe cramps in the abdomen which kept him from work for three or four days. Another spell of cramps lasting one day occurred two weeks previous to the present illness. Otherwise, the patient had never had any gastrointestinal symptoms, such as, hunger pain, after meal distress, heartburn, etc.

Examination revealed a well nourished adult male in severe pain. Pulse and temperature were normal. There was marked board-like generalized rigidity of the abdominal muscles with maximum tenderness in the region of the umbilicus and to the right of this area. Liver dullness was not obliterated. His blood count showed 10,200 white blood cells, 70 per cent polymorphonuclears, 10 of which were nonfilamentous. Urine examination was negative. A preoperative diagnosis of an acute condition of the abdomen with ruptured abdominal viscus was made.

Three hours after onset of symptoms operation was performed under spinal anesthesia. A right midrectus incision was made and the abdomen was opened in layers. On opening the peritoneal cavity there was a considerable

\* From the Surgical Department of the Highland Park General Hospital, Highland Park, Michigan.

amount of exudate covering the loops of the small bowel. Dark brown fluid was found in the right iliac fossa and seemed to be welling up from the pelvis. The appendix was found covered with the exudate, distended at its distal half and injected, but no perforation was noted. The meso-appendix was short and thick. Adhesions bound the appendix to the cecum. The ileum was explored for about thirty inches from the ileocecal junction and no diverticulum was found. As the pathological condition found in the appendix was not sufficient to account for the extensive exudative peritonitis, the incision was extended to the epigastrium. The gallbladder had its normal bluish color except that in places it was covered with the same exudate. The latter also covered the serous surface of the liver. However, in the pyloric region on the anterior surface of the stomach a punched-out opening was found about 2 cm. from the border of the greater curvature. The opening was about  $\frac{1}{2}$  cm. in diameter. The stomach wall surrounding it was moderately indurated.

Appendectomy was performed. Two guy sutures were placed at the greater curvature on either side of the perforated ulcer. An intestinal purse-string suture was used to close the opening. This was reinforced by a row of mattress sutures placed in the transverse diameter of the stomach. The end of the omentum was then anchored over the line of sutures. A cigarette drain was placed at the pyloroplasty and brought out through the upper apex of the incision. A similar drain was inserted in the pelvis and brought out through a stab wound in the right lower quadrant. Five Gm. of sulfanilamide were placed in the peritoneal cavity. The abdomen was closed in layers.

There was a distended appendix  $5 \times 1$  cm. The wall appeared edematous and the lumen contained blood. There was diffuse exudative infiltration of the appendiceal wall. (Fig. 1.)

*Microscopic diagnosis:* Acute purulent appendicitis.

Wangansteen suction was begun immediately after the operation and continued for five days. After a slightly elevated temperature for the first four days, it became normal and stayed so throughout the rest of the convalescence. The pulse and respirations were normal throughout. The drains were removed on the seventh postoperative day. The patient was

discharged from the hospital on the sixteenth day with the wound healed by first intention.

In studying the reports of the other nine cases, few striking findings were encoun-



FIG. 1. Diffuse exudative infiltration of appendiceal wall.

tered. All cases reported, with the exception of Andre's<sup>2</sup> case, occurred in males. The age of the youngest patient was fourteen years, and the oldest was sixty-seven years.

In the history of these patients we find that four of them, with the exception of having very short and rare spells of indigestion or cramps, did not have any signs and symptoms of peptic ulcer. During the acute attack most of the patients were known to have vomited once, while the nausea continued, so that one is justified in concluding that the stomach was emptying itself intraperitoneally. The location of the pain in all of the cases reported was chiefly in two areas: the epigastrium and the right lower quadrant or the right perumbilical region. However, in three cases the pain was found only in the right lower quadrant.

The preoperative diagnosis in practically all of the cases was acute appendicitis with or without peritonitis.

The anesthetic used was spinal in two cases and general in five. In four reports the type of anesthesia was not mentioned. With the exception of one case, the procedure was appendectomy, extension of the incision to the epigastrium, and simple

closure of the perforation with a tag of omentum anchored to it. In Scalfi's<sup>19</sup> case a posterior gastroenterostomy was carried out in addition to the closure of the perforation.

There were six anterior prepyloric perforations and four perforations of the duodenum. In one case of Pascali and Rodriguez-Ramos<sup>16</sup> the perforated ulcer occupied part of the pylorus and part of the duodenum. All but one of the cases reported, including the author's were drained.

During the period of convalescence, two cases developed complications. Serra's<sup>20</sup> case showed a rise in temperature and pulse and leucocytosis on the seventh postoperative day. The only finding was a positive Widal in 1:40 and 1:80 dilution (typhoid fever). Under appropriate measures (quinine and neoprontosil), the patient recovered and left the hospital cured. In the other case, reported by Scalfi,<sup>19</sup> in which a gastroenterostomy was performed in addition to the closure, the patient developed pneumonia and was taken home by his relatives in a moribund condition.

That peptic ulcer is a much more common disease than is clinically diagnosed is proved by autopsy statistics. Portis and Jaffee<sup>17</sup> (1938) report the finding of 457 cases of peptic lesions in 9,171 autopsies performed between June 1, 1929, and December 31, 1936, a total incidence of about 5 per cent. In these 457 cases, peptic ulcer was the essential lesion in 118, and in 221 it was the incidental lesion. They also found that when peptic ulcer was the essential lesion the duodenal localization predominated. In studying the incidence of perforation of peptic ulcers in North America, Brown<sup>5</sup> found that about 5 per cent of the ulcers perforate acutely, while chronic or subacute perforating ulcers constitute 25 per cent of cases of ulcer. In a series of 33,439 cases of gastroduodenal ulcers collected from the literature, DeBakey<sup>6</sup> found that there were 4,410 (13.2 per cent) cases of perforation. In a detailed study of 500 cases in 1937, Thompson<sup>22</sup>

reported that acute perforated peptic ulcer occurred predominately in the male (94.2 per cent).

The question arises in this series of cases: Which of the two conditions was primary, the appendicitis or the perforated ulcer? In support of the assumption that the patient had a peptic ulcer without the signs and symptoms thereof long before the development of acute appendicitis, we find a statement by Steward<sup>12</sup> who believes that the process of peptic ulceration from the onset to the time of complete perforation of the muscular coat occupies at least two months.

On the other hand, Mahmert,<sup>14</sup> as early as 1907, was the first to render evidence that inflammation of the appendix plays an important rôle in producing certain peptic ulcers. Pascalis and Rodriguez-Ramos,<sup>16</sup> from observation as well as experimental studies on dogs, conclude that an ulcer once found in the pyloric region gives rise to the inflammation of the appendix either through the peritoneal route, i.e., by contact, or through the lymphatics, or the infected material from the peptic ulcer reaches the lumen of the appendix through the digestive tract.

Among those who believe that the reverse is true, namely, that it is the presence of appendicitis that gives rise to the formation of peptic ulcer, we find M. P. Brodin and Mme. Tedesco.<sup>4</sup> They prove their contention by the distribution of the lymphatics: "The lymphatics of the appendix, ileum, and the cecum cross the third portion of the duodenum and, at the same time, the mesenteric vessels. The inflammation of these lymphatics provokes a spasm and to a greater degree a compression of the duodenum with the arrest of food at that level, and the appearance of duodenal stasis with dilatation of its inferior portion. This stasis alters profoundly the duodenal function by favoring infection and modifying the normal chemistry of the chyme at this important cross-road. The result of this mechanical infection and chemical alteration is an ulcer."

There seems to be more or less agreement as to the mechanism of perforation of the peptic ulcer in the presence of an acutely inflamed appendix. According to Almgovzen,<sup>1</sup> Scalfi,<sup>19</sup> Pascalis and Rodriguez-Ramos,<sup>16</sup> and Girand<sup>10</sup> the perforation is due to the spasm and active reverse peristalsis which is associated with acute appendicitis.

The pathological report, of course, was limited to the microscopic findings in the appendix and varied from that of acute appendicitis to that of gangrenous appendicitis.

In comparing the physical findings of this series of cases, one cannot select a definite set of signs and symptoms which would differ from the one we usually find in an episode of a ruptured abdominal viscus modified by the presence or absence of general peritonitis. However, we do find in the majority of the series reviewed that the pain of which the patients complained was in two areas of the abdomen, the right upper quadrant and the perumbilical region. In Flandin's<sup>9</sup> patient a roentgenologist diagnosed a "pathological appendix" two years before the last episode. But the patient was advised that "chronic appendicitis does not predispose to acute attacks. Therefore, no immediate operation is indicated."

In general, it may be said that the clinical signs and symptoms of an acute condition of the abdomen may be caused by a number of pathological conditions other than acute perforated ulcer alone or combined with acute appendicitis, but regardless of the underlying cause surgical intervention is imperative. In this regard Moynihan<sup>15</sup> put it quite aptly: "To make an anatomical and pathological diagnosis is a delight; to reach a decision that wherever and whatever the trouble the sooner measures of rescue are adopted, is a cardinal obligation." That the lapse of time between the perforation and the operation is one of the most important factors is emphasized by every author writing on this subject. Blackford and Baker<sup>3</sup> in an analysis of 933

cases of perforated peptic ulcer found that the mortality in the second twelve-hour period is double that of the first and that after the twenty-four-hour period it was more than four times as great. Harold L. Thompson<sup>21</sup> analyzes 500 cases of acutely perforated peptic ulcers. These were collected from the Los Angeles County General Hospital from September 9, 1921, to June 30, 1934. The operations were performed by fifty-seven surgeons. He concludes that "the gross mortality is around 40 per cent; that the mortality is lowest when operation is performed within six hours after perforation occurs, when the operation consists of suture of a tag of omentum over the closed perforation." This conclusion is well borne out by the mortality in this series. The only death occurring is the case in which a gastro-enterostomy was done in addition to the simple closure and appendectomy.

On the other hand, in one of the patients of Pascalis and Rodriguez-Ramos<sup>16</sup> the perforated ulcers had penetrated into the pancreas. The adhesions were very dense. The surgeon closed the perforation without loosening the stomach from the mass of adhesions. On discharge the patient was advised to return for a gastric resection in the near future. Three months later the patient was symptom free. The roentgenologist reports "a freely movable, pliable stomach with normal peristaltic waves and no evidence of ulcer," thus pointing to a cure without further interference. The same was true of the other three cases in their series. Although some of them showed marked adhesions at the operation, they all recovered completely with normal anatomic and physiologic function. Graham<sup>11</sup> thinks that additional procedures are "meddlesome and unnecessary." Ross<sup>18</sup> reports the follow-up data of eighty-nine out of a personal series of 175 cases of perforated ulcer in which simple closure was used. The follow-up suggests that, provided the patient adheres to a strict diet for six months after operation and maintains dietetic care thereafter, his prospects

of cure are good. In a collected series of 1,525 cases of simple closure, DeBakey<sup>7</sup> reports that 65 per cent remained symptom free and 35 per cent continued to complain. Of the latter 16.9 per cent required subsequent operation. At this writing the author's patient (three and one-half months after the operation) has gained weight on a well balanced, ulcer-restricted diet, is free from symptoms, and continues his former gainful occupation.

#### CONCLUSIONS

1. A case of perforated peptic ulcer complicated by acute appendicitis is reported. Nine other such cases found in the literature are analyzed.

2. No age is exempt from being affected with acute appendicitis and perforating peptic ulcer.

3. A history of previous digestive disturbances is frequently missing.

4. The pain of which the patient complains is often located in two areas, the right upper quadrant and the right lower quadrant.

5. Liver dullness does not always disappear in perforating peptic ulcer.

6. The preoperative diagnosis in all the cases reviewed was acute appendicitis with or without perforation, and only postoperatively was the co-existence of the two lesions found.

7. The right rectus incision is the best suited for an acute condition of the abdomen with maximum tenderness in the right side. It allows, when indicated, an easier exploration of the abdominal contents.

8. When the pathological condition in the appendix is not sufficient to account for the extensive peritonitis present, it is imperative to search for another lesion in the abdomen, especially in the gastro-duodenal region.

9. The wisdom of a long established rule, to operate whenever a diagnosis of appendicitis, acute or chronic, is made is reaffirmed by some of the cases in this series.

10. The mortality and results are best when the operation consists of appendectomy and simple closure of the perforation with a tag of omentum anchored to it. A number of these patients when re-examined months later were found symptom free with normal anatomic and physiologic function.

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# BLASTOMYCOSIS OF CECUM\*

## CASE REPORT

GEORGE F. THOMPSON, M.D.,

Senior Attending Surgeon, St. Anne's Hospital

M. J. SULLIVAN, M.D.

Member of Junior Staff, St. Anne's Hospital

AND

PAUL F. FOX, M.D.

Senior Attending Surgeon, St. Anne's Hospital

CHICAGO, ILLINOIS

**B**LASTOMYCOSIS was described independently in 1894 by Gilchrist<sup>1</sup> and Busse.<sup>2</sup> The disease is caused by the blastomycete, a yeast-like organism which multiplies by budding in tissue but develops mycelial threads when growing in culture.

The part of the body usually infected is the skin where ulcerating lesions form. The disease may remain local or become systemic, invading the lungs, liver or gastrointestinal tract. Occasionally, it is primary in these organs. In addition to these sites, the organism has been found in the larynx, trachea, pleura, myocardium, spleen, pancreas, kidneys, adrenal glands, lymph-nodes, bones, joints, brain, spinal cord, urine, feces, sputum, blood, spinal fluid and prostatic secretion. The papers of Goto,<sup>3</sup> Hurley,<sup>4</sup> Stober,<sup>5</sup> Montgomery and Ormsby,<sup>6</sup> Powers,<sup>7</sup> and Wade and Bel,<sup>8</sup> are concerned with the various systemic manifestations of the disease.

An interesting observation is that the majority of the infections due to blastomycosis have been reported from the Chicago area. However, the disease has occurred in other states in the United States, South America, Canada, the British Isles, Continental Europe, India and Japan. Most of the patients have been males in the third decade of life and many of the American cases apparently showed a relationship to poor environment, hard work, and exposure, according to Sihler, Peppard, and Cox.<sup>9</sup>

Our patient was unusual in several respects. He had, as far as we were able to determine, no other lesion of blastomycosis except in the cecum. There was no skin infection, roentgenographic evidence of pulmonary involvement was lacking, and abdominal exploration at the time of operation revealed no other site in the gastrointestinal tract or abdominal viscera. Complete extirpation of the cecum and terminal ileum has apparently produced a cure. Finally, he was well above the average age of the other patients reported to have the disease.

The patient reported by Sihler, Peppard, and Cox<sup>9</sup> was found at postmortem examination to have blastomycetes in the stomach wall, liver, lymph-nodes, urinary bladder wall, omentum, appendix and ascitic fluid. This patient also had an ulcer of the stomach with the organisms in the ulcer wall. The conclusion was that the stomach wall was the portal of entry. From this it may be seen that the disease was quite widespread in the abdominal cavity and contrasts sharply with our patient who seemingly had a well localized infection. Harter<sup>10</sup> and Okake<sup>11</sup> also reported patients with widespread abdominal involvement.

## CASE REPORT

P. W., a white, male, aged seventy-four, (Hospital No. 40-4456) was seen on April 20, 1940, by M. J. S. at his home. His complaints at that time were anorexia, vomiting at irregular intervals, abdominal distention, pain across

\* From the Department of Surgery, St. Anne's Hospital, Chicago, Illinois.

the lower portion of the abdomen and alternating constipation and diarrhea. These symptoms had been present for ten days.

Physical examination revealed a tall, thin, patient, not acutely ill, with a moderate amount of abdominal distention and a tender movable mass in the right lower abdominal quadrant about the size of a lemon. Hospitalization was advised and on April 22, 1940, the patient was admitted to the hospital.

His past and personal history was not particularly significant. A complete recovery following a skull fracture in 1938 was noted, and a hemorrhoidectomy had been performed in 1930. He had lived in Chicago for the past forty years and was a building contractor.

On admission he appeared much the same as he did two days before at his home. The physical findings were essentially the same although a fever of 100°F. was observed. Urine analysis showed an occasional pus cell and epithelial cell. A blood count revealed the hemoglobin to be 10 Gm., erythrocytes 3,500,000 with slight anisocytosis, poikilocytosis, and polychromatophilia, leukocytes 9,600, of which 21 per cent were lymphocytes, 4 per cent large mononuclears, and 75 per cent neutrophils.

Roentgenographic studies were made on April 23, 1940, the day after admission to the hospital. The heart and lung fields showed no unusual changes. Barium enema revealed a redundant and tortuous colon. The right side of the colon was not well visualized and there appeared to be a filling defect corresponding to the site of the palpable mass (in the right lower quadrant), however, after evacuation and injection of air the appearance of the cecum and ascending colon was considerably changed. Therefore, it was decided to attempt to visualize the cecum by using barium per mouth on the following day. In addition to this change there were several large and small diverticuli in the sigmoid and ascending colon.

The next day, April 24, 1940, roentgenographic studies showed no intrinsic lesion in the stomach or duodenum. There was no delay in the passage of barium through the duodenum, and at four hours the stomach was empty with the barium distributed throughout the distal ileum and proximal portion of the colon. At this time there appeared to be a filling defect in the cecum corresponding to the site of the palpable movable mass. At twenty-four hours the same defect in the cecum was visualized and the

inference by the roentgenologist was that a neoplasm of the cecum was present.

For the next few days attention was directed toward preoperative measures and on April 29, 1940, operation was performed.

Under inhalation anesthesia a right lower abdominal paramedian incision was made. A freely movable, hard, round, tumor mass about the size of an egg adjacent to the proximal portion of the appendix was palpable in the cecum. The appendix was short and thick and intimately adherent to the cecum. The anterior surface of the cecum was covered by omentum which was densely adherent. Suspecting that this segment of the adherent omentum indicated the presence of a threatened or actual perforation of the cecum, it was ligated and cut between two ligatures. Later examination of the specimen revealed a perforation 3 mm. in diameter underneath this adherent omentum. A resection of the cecum and ascending colon including the distal 10 cm. of the ileum was then effected. Blind-end closure of the transverse colon with an end-to-side ileocolostomy completed the intestinal surgery. One cigarette drain was placed in the colonic gutter and closure in layers performed.

The pathological report was as follows: The specimen consisted of 15 cm. of cecum, 10 cm. of ileum, and appendix. The bowel and appendix had been split open. At the base of the appendix there was considerable congestion and induration with ulceration and perforation on the anterior wall of the cecum. Microscopic sections reveal chronic granulomatous inflammation due to blastomycosis.

The postoperative course was quite uneventful except for a moderate amount of purulent drainage which persisted for approximately four weeks. At no time was fecal drainage noted. Fever which ranged between 99 and 100°F. was present for two weeks. The patient left the hospital thirty days after operation and soon regained his normal strength. He has had no symptoms referable to the gastrointestinal system following his recovery from the operation.

#### COMMENT

We believe that a separate, isolated infection due to blastomycosis in the cecum is of very rare occurrence. In fact, no other similar case has been reported to our knowledge.

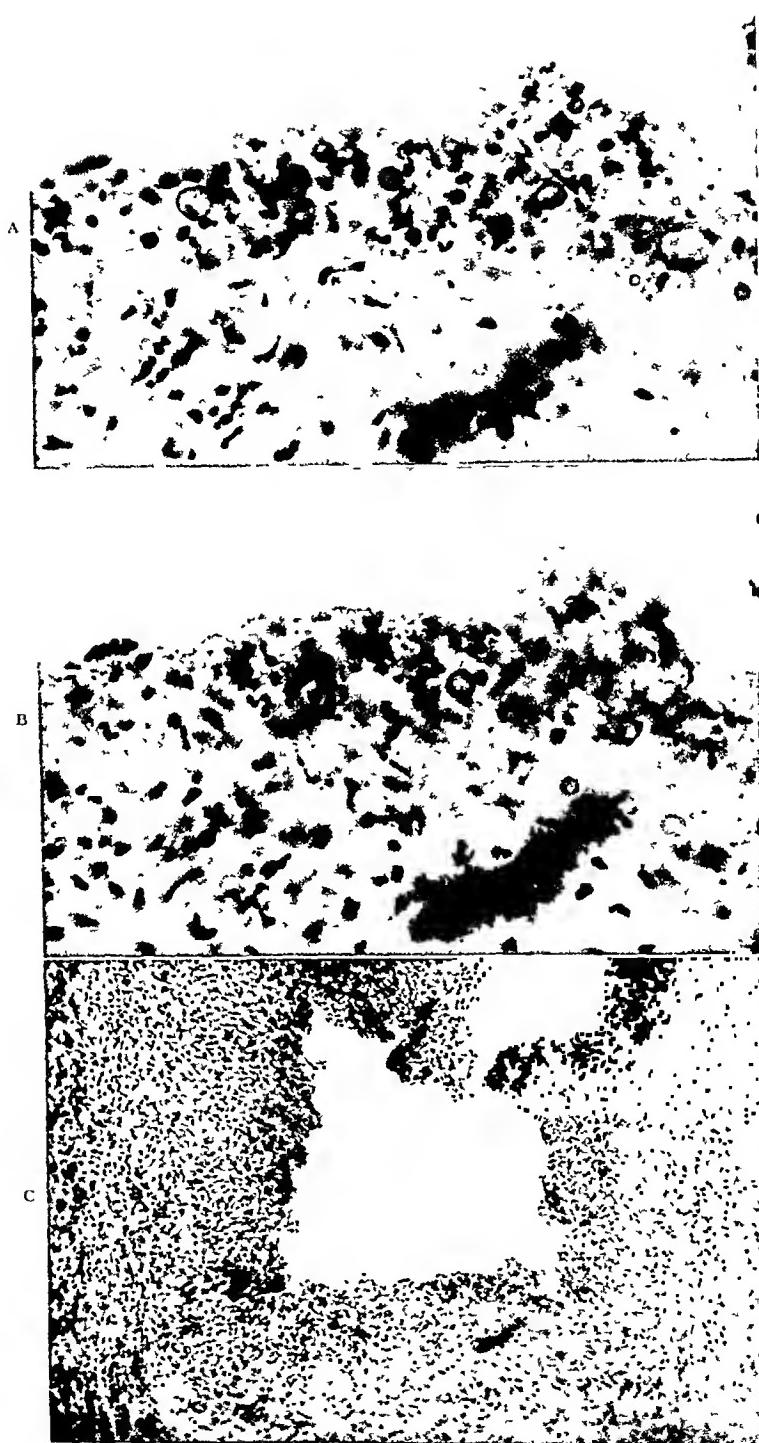


FIG. 1. A, photomicrograph of section of wall of cecum showing blastomycetes— $\times 630$ . B, photomicrograph showing spherical refractile (wall of cecum) blastomycetes— $\times 630$ . C, photomicrograph (low power) showing section of cecum; same as in A and B.  $\times 155$ .

This patient has apparently been cured by a one-stage operation consisting of resection of the terminal ileum, cecum and ascending colon, and performance of an ileotransverse colostomy.

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SUPERNUMERARY breasts (polymastia) usually appear as small nipples below the breasts in the "milk line." Sometimes they are so small as to resemble pigmented moles. Occasionally miniature breasts are seen. Usually not more than one or two are present, but cases have been reported with as many as ten.

The brief excerpts in this issue have been taken from "Plastic Surgery of the Breast and Abdominal Wall" by Max Thorek (Charles C. Thomas).

# SPLANCHNICOTOMY IN A SIX-YEAR OLD CHILD WITH MARKED HYPERTENSION\*

AMIL C. BACH, M.D.  
INDIANAPOLIS, INDIANA

AND

KNIGHT ALDRICH, M.D.  
LEXINGTON, KENTUCKY

RELIEF of the distressing symptoms associated with far advanced hypertension has been shown to be a more frequent result of operations on the splanchnic nerves than is long standing lowering of the blood pressure.<sup>1</sup> It is believed, however, that even when there is little probability of increasing the life span of these unfortunate individuals, a procedure which permits them to spend their last days in relative comfort is justified. One of the criteria for the choice of subjects for surgery is the youth of the patient; with this case of a six-year old child we believe we are reporting the youngest individual on whom a splanchnic operation has been performed for hypertension.

## CASE REPORT

A six-year old, white female entered the Children's Service of Cook County Hospital on March 10, 1940, with complaints of headache, vomiting and stiff neck of two days' duration. She was a lethargic, irritable child whose family gave a history of intermittent attacks of convulsions over a period of three years. Investigation showed that she had been seen sixteen times in the previous two years in out-patient clinics and had been hospitalized three times for convulsive attacks. Some of these started in the foot, spread to the arm and face on the same side and lasted from twenty minutes to two hours. Among the laboratory data uncovered from examination of her past history no blood pressure recording could be found. She had questionable positive Brudzinski and Kernig signs. The left pupil was slightly larger than the right although both reacted well to light. There was a loud, snapping aortic second sound and a systolic murmur heard best in the third left interspace. The liver was palpable two finger breadths below the costal margin. Blood pressure was 238/180

on all extremities. The urine consistently showed 4 plus albumin, with many cells and hyaline casts; specific gravity ranged from 1.010 to 1.020. The pressure of the spinal fluid was increased and there were 100 cells per c. mm. of fluid and a three plus pandy test. Hemoglobin was 14 mg., white blood count 18,400, blood nonprotein nitrogen 30 mg. and total protein 7.81 mg. (albumin-globulin ration was 6.25/1.56. X-rays of chest, abdomen and skull were negative and on March 27 a retrograde pyelogram was normal. Eye-ground examination showed several small areas of degeneration. The vessels were small but no "crossing phenomena." Cystoscopy reported hypertrophy of interurethral ridges with bulbous edema of both ureteral orifices. The patient did not derive benefit from treatment with magnesium sulfate or hypertonic fluids but remained semicomotose, incontinent and vomited frequently, so a splanchnicotomy was suggested and performed by Dr. Verbrugghen.

The left side was done on April 5 and the right on April 19. The patient developed a right upper lobar pneumonia following the second operation but recovered uneventfully and her blood pressure which had never been below 200/160 preoperatively, gradually fell to 160/110 by May 5, and then began to rise again. Symptomatically she was much improved, more alert, cheerful and bright, with only occasional nausea and no vomiting. By May 16, although her blood pressure was 190/120, her general condition was excellent and plans were made to send her home. At this time her urine showed 1 to 2 plus albumin, with specific gravity varying between 1.007 and 1.013 and her blood nonprotein was 35. She began again to vomit and ran a steady downhill course, became stuporous and expired June 8, 1940.

Postmortem examination revealed a poorly developed, poorly nourished, white female, 127 cm. in length and weighing 20 kg. There were two recent surgical scars over the back at the

\* From the Departments of Pathology and Neurosurgery, Cook County Hospital, Chicago, Illinois.

level of the eleventh thoracic vertebra bilaterally and a supernumerary digit on the left foot. The pericardial sac contained about 40 cc. of clear yellow fluid. The heart weighed 180 Gm. The myocardium was very firm and the wall of the left ventricle measured 16 mm. and the right 4 mm. in thickness. There were many small fatty and hyaline placques on the membranous endocardium of the left ventricle, the free margins of the aortic and mitral valves were slightly thickened and the left ventricle was moderately dilated. The coronaries and aorta were essentially negative. There was a chronic passive congestion of the liver, spleen and an aberrant spleen. The latter measured 26 by 15 by 12 mm. The kidneys weighed 165 Gm. together. The left was slightly smaller than the right. The capsule stripped with slight difficulty leaving a coarsely granular, light purple and grayish tan surface with an occasional depression 6 mm. in length and 2 mm. in depth. On sectioning, the cortex averaged 4 mm. in width, was light purplish tan and the markings were distinct. The medulla appeared to be normal. Both renal arteries measured 3 mm. in diameter at their points of origin.

The vagina was divided into two separate and distinct parts by a thick, firm, longitudinal septum. Each vagina connected with a separate and independent cervix and uterus. Each uterus had only one tube. (Double vagina and bicornuate uterus.) The uterus measured 33 by 15 by 7 mm. Both Fallopian tubes were patent and the ovaries were small. The thyroid, pancreas, adrenals and pituitary were essentially unchanged. The brain weighed 1,060 Gm., it was edematous, the convolutions were flattened, the meningeal vessels were congested, and there were small multiple intermeningeal hemorrhages over the frontal and occipital lobes. The left lateral ventricle was moderately dilated and contained about 30 cc. of clear fluid. The third ventricle appeared to be normal. The white matter was congested. The vessels at the base of the brain contained scattered fatty and hyaline placques.

Microscopic examination revealed a slight perivascular, round cell infiltration in the meninges and white matter and a moderate hyperplasia of the intima and media of the arteries and arterioles in both the meninges and cortex. The general cyto-architecture of the cortex was preserved and no significant gliosis was noted.

Muscle fibers of the heart were markedly hypertrophied, cross striations were indistinct, cytoplasm was light pink and granular and the nuclei were barrel shaped.

The architecture of the kidney was well preserved. The glomeruli were swollen and filled Bowman's capsule. There was slight to moderate proliferation of the endothelial cells of the capillary tufts and the latter were moderately congested with red blood cells. There were several partially to completely hyalinized glomeruli scattered throughout and an occasional epithelial crescent was present. Bowman's capsule was slightly to moderately thickened. The interstitial capillaries were markedly dilated and filled with red blood cells. The tubular epithelium was swollen and granular and the lumina contained cellular débris and numerous hyaline casts. The small arteries and arterioles showed marked thickening of the intima and media, some to the point of occlusion of the vessel, and there was a moderate increase in interstitial connective tissue. There were focal accumulations of round and plasma cells, especially near the hyalinized glomeruli. Sudan III stain revealed a moderate to marked deposition of sudanophilic droplets in the tubular epithelium, the hyalinized glomeruli and in the intima and media of the small arteries and arterioles.

Microscopically the pituitary, thyroid and adrenal gland were normal.

The anatomical diagnosis was as follows: Chronic glomerulonephritis; marked eccentric hypertrophy of the heart with dilatation of all cardiac chambers; slight fibroplastic deformity of the aortic and mitral valves; marked edema and passive congestion of the brain and moderate internal hydrocephalus on the left side; passive congestion of the lungs, liver, spleen and kidneys; parenchymatous degeneration of the heart, liver, and kidneys; stasis catarrh of the gastrointestinal tract; uremic injection of the small intestine; bicornuate uterus and double vagina; aberrant spleen; supernumerary digit of left foot; recent healed surgical scars at level of eleventh thoracic vertebrae bilaterally.

#### DISCUSSION

Splanchnicotomy was first introduced for the relief of hypertension by Pender,<sup>2</sup> in 1924, and according to Martin's compe-

hensive review of the literature<sup>3</sup> "is rapidly growing in popularity and if one may judge by results stated in reports, is offering more hope for a solution than any form of surgery yet described." Craig and Allen<sup>4</sup> as well as many other authors have pointed out that in far advanced cases the effect of surgical procedures is neither marked nor lasting. However, the extent to which symptoms are relieved, as reported by Crile<sup>5</sup> and others, would seem to justify the procedure in selected cases, especially since the mortality is very low. Although the kidney is apparently the chief etiological factor in a large proportion of cases, Mosenthal and Lander<sup>6</sup> have shown that it is difficult to determine whether the hypertension is primary or secondary to the renal picture. Keith et al.<sup>7</sup> believe that vasoconstriction is the constant factor in the different types of hypertension. Even though developmental anomalies were presented in this case, we do not believe that they contributed to the cause of the hypertension. However, it is possible that some further anomalous condition may have escaped detection at autopsy especially since no examination of the spinal cord could be made, and the renal pathological

status might have been secondary to hypertension caused by such a condition.

#### SUMMARY AND CONCLUSION

A case of a six-year old girl with a three-year history of convulsions and a blood pressure of 238/180 was temporarily symptomatically improved by bilateral splanchnicotomy. This is the youngest recorded case of its kind.

Splanchnicotomy may give symptomatic relief in far advanced cases of hypertension due to chronic nephritis.

Blood pressure readings should be taken in all children subject to convulsive attacks.

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# DOUBLE MALIGNANCY: HYPERNEPHROMA AND BASAL CELLED CARCINOMA OF NOSE\*

## REPORT OF CASE

CHARLES PIERRE MATHÉ, M.D. AND

Director of Department of Urology, St. Mary's Hospital

SAN FRANCISCO, CALIFORNIA

CHARLES F. STEISS, M.D.

Plastic Surgeon, St. Mary's Hospital

THE multiplicity of primary malignant tumors occurring in different organs of the body is of great interest to the medical world. We report a case of multiple cancer in which nephrectomy was performed for hypernephroma. Three years later the patient developed basal celled carcinoma of the nose requiring removal. The cancerous lesions involving the kidney as well as those of the nose presented the characteristic pathological picture of well recognized neoplasms that commonly involve these organs. There was no metastasis from either primary cancer and each was individually cured by radical extirpation of the kidney and of the nose. By virtue of a series of plastic operations the nose has been entirely reconstructed. Over a period of fourteen years there has been no recurrence of kidney cancer nor any evidence of metastasis to other organs. The patient has not only been definitely cured of cancer and restored to good health but her nose has been so well reconstructed that she is now a presentable member of society. This case is indeed a living testimonial to the efficacy of radical surgical removal of cancer when it is found to exist in the vital organs of the body.

A number of cases presenting multiple cancer have been published. In 1940, Shapiro and Bolker reported an interesting case presenting co-existent triple primary neoplasms consisting of lymphosarcoma of the right inguinal region, adenocarcinoma of the right kidney and papillary adenocarcinoma of the colon. White explains the

genesis of primary multiple cancers on the basis of the interaction of a functionally matured gene bearing the unit character for cancer inheritance with a functionally matured gene bearing the unit character for localization in various structures. He points out the fact that in cases of multiple cancer there must be definite, distinct and invasive new growths presenting the macroscopic and microscopic characteristics of the morphologic features of independent cancers, the cells of each type being equally capable of forming characteristic metastasis.

## CASE REPORT

A female, aged thirty-six, Case No. 49547, referred by Dr. Wm. Fritsch, entered St. Mary's Hospital January 4, 1928, for diagnosis and treatment of painful swelling in the left upper abdominal quadrant. In 1914, she suffered from general debility. This continued and in 1924 appendectomy was performed without improvement of her condition. In 1924, the patient underwent cholecystectomy for cholecystitis. In 1927, she noted fullness in the left upper abdominal quadrant and lumbar region. Since that time she suffered from dull non-radiating pain in the left loin. At times there would be nausea but this was not accompanied by vomiting. She noted hematuria on two occasions and, other than occasional nocturia, she complained of no other urological symptoms. The patient ran an intermittent fever, the temperature varying from 98° to 101° F.

The heart and lungs were negative. In the upper left abdominal quadrant a smooth tender mass was palpated. It extended into the kidney fossa and moved freely with respiration.

\* From the Departments of Urology and Plastic Surgery, Saint Mary's Hospital, San Francisco, California. Read before the monthly clinical staff meeting of St. Mary's Hospital, San Francisco, September 18, 1941.

Laboratory examination of the blood revealed the following: hemoglobin, 85 per cent; erythrocytes, 4,790,000; leukocytes, 14,500; small

siderable distortion. (Fig. 1.) The upper major calyx was irregular and elongated and presented a pressure defect of the lateral wall. It com-

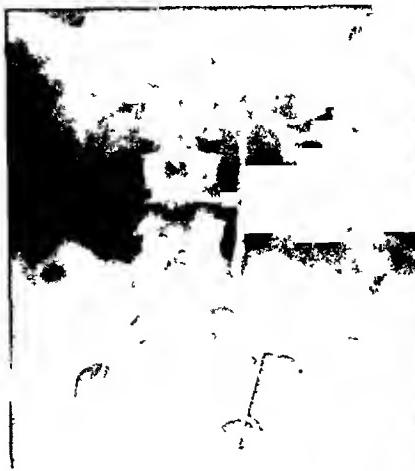


FIG. 1. Ureteropyelogram showing marked distortion of the kidney pelvis. In addition to elongation and to pressure defect of the lateral border of the upper major calyx there is extravasation of the opaque medium into an irregular cavity involving the upper pole.

lymphocytes, 14; monocytes, 10; and neutrophiles, 76. The blood Wassermann test was negative.

The urine was found to be turbid; reaction, acid; specific gravity, 1.027; albumin, trace; and sugar, negative. Microscopic examination revealed heavy strands of mucus, 4 to 6 leukocytes to the high dry field, erythrocytes 50 to 60 to the high dry field and no organisms. Phenolsulphonephthalein test (intramuscular) 80 per cent of the dye recovered in two hours.

A complete kidney examination was made including cystoscopy, catheterization of the kidneys, renal function tests and microscopical examination of the urines including cultures. Our studies revealed moderate staphylococcal infection of the left kidney and bladder as well as diminished function of the left kidney.

In addition, a roentgenological examination was made. Fluoroscopy of the heart and lungs and x-ray films of the gastrointestinal tract revealed negative findings. Flat kidney films showed considerable irregular enlargement of the left kidney. Bilateral retrograde pyelograms were made. The right kidney pelvis appeared normal. The left kidney pelvis presented con-



FIG. 2. Photograph of sagittal section of kidney removed by operation demonstrating large hypernephroma of the left kidney containing a large necrotic cavity.

municated with an irregular cavity involving the upper pole measuring 4 em. in diameter. The middle calyx was considerably elongated and flattened and extended laterally for a considerable distance. In taking the pyelogram in the upright position, considerable descent of both kidneys was observed.

The diagnosis of cancer of the left kidney was made and it was decided to carry out nephrectomy immediately. In reviewing the pyelograms we endeavored to explain the cavity that existed in the upper pole of the left kidney. This could well have been due to abscess formation, in view of the leukocytosis of 14,500 and the fact that the patient was running a fever. In studying the pyelogram taken in the vertical position it was noted that there was an appreciable descent of the kidney. The absence of renal fixation—the author's (Mathé) positive roentgenographic sign for kidney and perinephritic abscess—ruled out suppuration in the renal parenchyma in this case.

Nephrectomy was performed on January 20, 1928, through the usual lumbar incision. The kidney was found to be considerably enlarged, about three times its normal size, due to a tumor involving the upper pole. The renal pedicle was deliberately clamped early in the

operation and the kidney carefully dissected free from the surrounding tissues in order not to force any of the cancerous cells into the renal

often encountered in the line of demarcation between necrotic and actively growing tissue. The structure of the tumor near the kidney



FIG. 3. Basal cell carcinoma of the nose; duration approximately eight years. Surgery advised at this time, December, 1939, but treatment refused.



FIG. 4. Showing the appearance of the carcinoma in August, 1940. Radium therapy has failed to control extension of the tumor.

vein nor to spill them into the incision. During the operation the tissues were gently handled and the wound was repeatedly washed with alcohol. The renal pedicle was triply tied *en masse* and the kidney removed.

Dr. Elmer Smith, pathologist, St. Mary's Hospital, reported the following findings: "The kidney presents a large yellow tumor of the upper pole, the center of which contains a necrotic cavity. The tumor mass exerts considerable pressure on the upper pole, almost completely replacing normal kidney tissue. The lower portion of the kidney appears normal. Microscopical sections of the tumor reveal that it is composed of fibrous-like tissue made up of spindle cells which have invaded the cortical substance of the kidney, causing almost complete atrophy of the tubules. A few tubules still remain in this region, however, they are markedly compressed. There are a few epithelial structures which appear to be active and resemble young glandular tissue. Reticulated round cells are found in that part of the margin of the tumor mass that has not undergone necrosis and contains a few leukocytes and wandering cells as well as blood pigment. In the margin, between the actively growing tumor and the necrotic area, one sees many dilated capillaries and hemorrhagic areas such as are

capsule resembles fibrosarcoma; however, small reticulated cells with small nuclei resembling those of the adrenal body are also present. Diagnosis: hypernephroma of the left kidney."

The wound healed in thirty days after which time the patient was given a course of post-operative radium therapy consisting of 5,000 mg. hours and discharged from the hospital free of pain and fever. While preparing a paper on cancer of the kidney, which was delivered before the Urological Section of the California Medical Association Meeting in May 1936, the patient was contacted in Chicago, Illinois, at which time recheck investigation revealed that she had been entirely relieved of her symptoms and was enjoying perfectly good health.

In 1932, the patient noted a small pimple on the nose which gradually increased in size and became ulcerated. Ointments were applied with no relief. In 1938, she consulted Dr. Monica Donovon who made a diagnosis of basal celled carcinoma and instituted radium therapy. After primary regression, radium seemed to lose its effectiveness and the carcinoma soon invaded the greater portion of the nose. Dr. Donovon, who has had wide experience in radium therapy, then advised surgical extirpation.

In December, 1939, one of us (C. F. S.) was called in consultation for the purpose of

surgically relieving this condition. At this time the tumor had involved the greater portion of the nose. (Fig. 3.) Biopsy revealed a typical

columella. The mucous membrane of the nose and the skin were sutured together at the margin of the defect that had been created thus



FIG. 5. Appearance of nose following surgical excision of the tumor. The forehead flap has been raised and delayed. Note the unfortunate pre-existing forehead scars.

FIG. 6. Appearance of the nose at the present time. Further work will be done to improve the cosmetic result. The forehead defect has been grafted with full thickness skin.

basal celled carcinoma. Careful examination showed that there was no metastasis in the neighboring glandular structures, however, the nasal lesion had extended into the alar cartilage, septum and columella. Surgical extirpation and subsequent plastic repair of the nose was recommended; however, the patient refused radical surgery and requested another course of radium therapy. This was instituted with the understanding that if there was no improvement, surgical intervention would be carried out.

In September, 1940, the patient was re-examined and it was observed that considerable growth of the cancer had taken place. (Fig. 4.) Fortunately, the palpable glands of metastasis were still absent and it was agreed to relieve this condition by surgical intervention with a full understanding of the radical nature of this procedure. A simple plan of attack was decided upon, namely, wide excision of the malignant lesion with disregard of consequent defect. After healing had occurred reconstruction surgery would be carried out, utilizing all available material and according to existing circumstances.

On September 16, 1940, under avertin and local anesthesia, the tumor was excised widely with the electric knife, including two-thirds of the nose and a portion of the septum and the

forming a closed wound. The patient made an uneventful recovery, the wound healed in four weeks, at which time the surgical problem of reconstruction was undertaken. (Fig. 5.)

We were now dealing with the problem of complete rhinoplasty since both the skin of the nose as well as its nasal lining had to be provided. As the patient was very nervous, a rapid and comfortable type of reconstruction operation was chosen, namely, the forehead flap. We elected this method of repair in spite of the fact that there were pre-existing scars on that portion of the forehead that was to be utilized in the flap and which would necessarily have to be transplanted to the nose. The first stage of this reconstructive operation consisted in the formation of a forehead and scalp flap that was formed in such a way that its pedicle would contain the right temporal artery. This flap was not immediately brought down to the nose, but was deliberately delayed by returning it to its original bed for the purpose of allowing the circulation to adjust itself. At the time of operation, flaps were also resected from the margin of the defect produced by removing the nose and these were turned inward in order to furnish a lining. These flaps were also delayed.

Three weeks later, the second stage of the operation was performed. This consisted of again raising the lining flaps and suturing them

to the freshened edges of the defect. The forehead flap was then superimposed on these lining flaps and sutured into place, forming the nostrils and columella with infoldings of pliable skin. The defect in the forehead formed by removing the flap was corrected by grafting a suitable sized portion of full thickness skin of the abdomen. (Fig. 6.)

Three and a half weeks later, the pedicle was severed and the scalp flap replaced into its original bed. In the meantime the full thickness graft had taken completely. After healing had occurred, a better cosmetic result was obtained by performing minor surgical adjustments which were deemed necessary. The pre-existing forehead scars can still be seen but the final result is indeed successful, *inasmuch as* the cancer has been completely removed and the nose has been successfully reconstructed.

#### DISCUSSION

This patient presented an unusual condition in the fact that she was afflicted by different types of cancer, viz., hypernephroma of the left kidney and basal celled carcinoma of the nose occurring independently and three years apart. She was cured of cancer by nephrectomy for hypernephroma in 1928 and by radical removal of the nose for basal celled carcinoma in 1940. She has shown no evidence of recurrence of kidney cancer in fourteen years. We realize that metastasis from renal neoplasms occasionally take place as long as twelve years after surgical removal, however, one can justly conclude that this patient has been definitely cured of kidney cancer because she is living and well four-

teen years after nephrectomy. The basal celled carcinoma of the nose failed to respond to radium therapy and was successfully relieved by radical excision, and the nose was subsequently reconstructed by a series of plastic operations. The patient has been restored to good health and is now a presentable member of society.

#### SUMMARY

1. We report a case presenting double primary neoplasms consisting of hypernephroma of the left kidney and basal celled carcinoma of the nose occurring independently and three years apart.

2. The patient presents a fourteen-year cure of kidney cancer. Early ligation of the renal pedicle, gentle handling of the kidney and sponging of the wound with alcohol sponges during nephrectomy and utilization of postoperative radium therapy aided in curing this patient.

3. The basal celled carcinoma of the nose, which had responded to radium therapy for a time, became radioresistant and required radical extirpation.

4. The nose has been successfully reconstructed by a series of plastic operations.

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# AVULSION OF THE ANTERIOSUPERIOR ILIAC SPINE\*

ASSOCIATED WITH OSTEOCHONDRITIS AND HYPOTHYROIDISM

ROSS SUTHERLAND, M.D.  
LOS ANGELES, CALIFORNIA

AND

M. JOHN ROWE, JR., M.D.  
LONG BEACH, CALIFORNIA

FRACTURES due to muscular force alone and particularly those of avulsion of the anteriosuperior iliac spine

## CASE REPORT

Our patient, a boy of fifteen, had been treated in this clinic several years previously for mild



FIG. 1. Original film showing fracture.

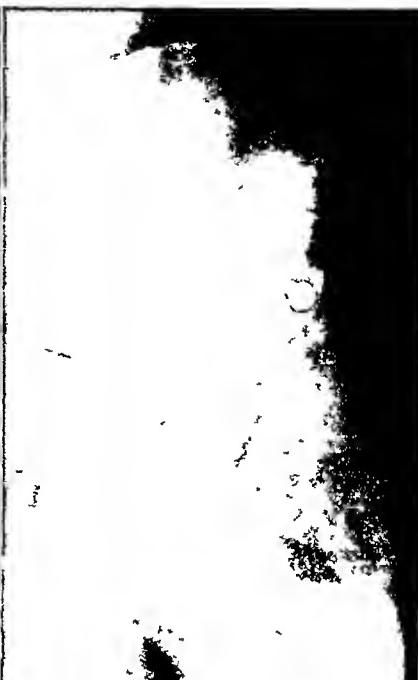


FIG. 2. Film three weeks postoperatively.

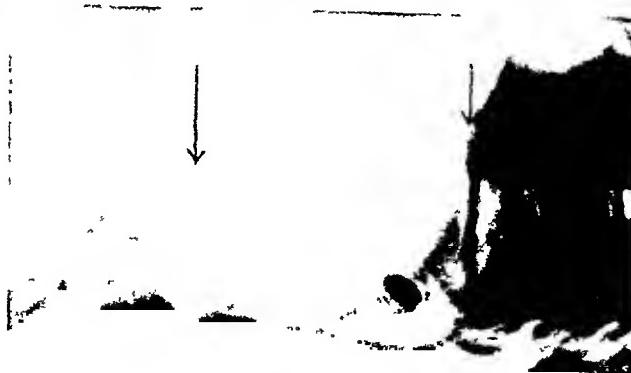


FIG. 3. Spine film showing irregularities due to osteochondritis.

are relatively rare. The possibility of predisposing bone weakness as an etiological associate of muscular violence has not, to our knowledge, been proposed.

osteochondritis of the calcanei and spine with thyroid medication. He had failed to return after subsidence of symptoms until two years ago. At that time he gave a history of sprain

\* From the Tichenor Orthopedic Clinic, Long Beach, California.

of the left ankle several weeks previously, which pain had not entirely subsided. X-rays revealed fracture of the left talus but clinical limitation of motion and pain were relatively slight, so surgical treatment was delayed until the condition warranted further therapy. He then did not return to the clinic or continue his thyroid medication until the present injury. At this time he was running, fell to the ground with a sudden severe pain in the left hip area and was unable to arise. There was marked tenderness over the fractured left iliac spine, crepitus was elicited and x-rays confirmed the diagnosis.

He was put to bed and seven days later because of continuing disability an open reduction was done of the separated fragment which was fixed in place with a vitallium nail and a mattress suture. A spica bandage was applied and he was kept in bed for three weeks. At that time the wound was well healed, full muscle function was present and painless, and callus was visible in the x-ray.

Laboratory studies made four weeks post-operatively were as follows:

Basal metabolic rate: -5 per cent on two separate determinations

Blood cholesterol: 168.2 mg. per cent. (Two years before while under thyroid therapy the blood cholesterol was 127 mg. per cent)

Blood calcium: 5.59 mg. per cent

Blood phosphorus: 3.91 mg. per cent

Blood phosphatase: 8.59 units

Blood sedimentation rate: 8 mm. in sixty minutes

Thus in this case there is mechanical imbalance in the leg from a distorted talus causing muscular violence which produces a fracture in an epiphysis having probably delayed growth and abnormal endocrine status which is substantiated by the lower basal metabolic rate. This endocrine factor may be the underlying cause in some of the fractures which are now given as caused solely by muscular violence.

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# GALLBLADDER FORCEPS FOUND IN THE ABDOMINAL CAVITY

## CASE REPORT

A. J. GUZZETTA, M.D.

Attending Surgeon, St. Mary's Hospital, and Monroe County Infirmary

ROCHESTER, NEW YORK

NUMEROUS cases have been reported of foreign objects found in the abdominal cavity days or months after an operation. In this patient, gallbladder forceps were found two years after the removal of the gallbladder. The patient was fairly comfortable until three weeks before entering the hospital. Her

and in distress. The abdomen was very obese and difficult to examine. Tenderness was present more on the left side than on the right. No spasm or rigidity was evident, but there was question of an ill defined mass in the right upper quadrant. No fluid or distention was present. A questionable liver edge could be felt three

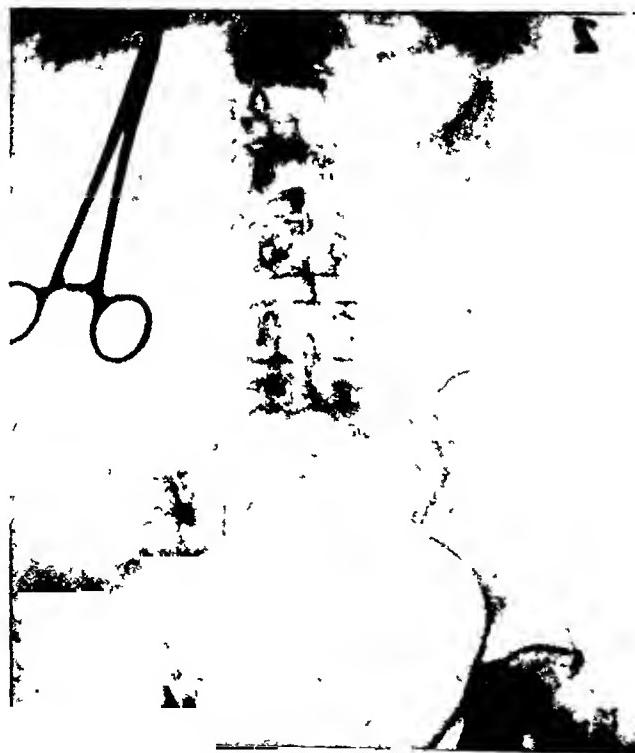


FIG. 1. Forceps in abdominal cavity.

chief complaint was a sharp, gripping pain on the right side near the costal margin radiating across the abdomen, one to two hours after meals. Fat did not increase the pain. The patient stopped eating fat on the advice of a physician. She was afraid to eat for fear pain would increase. Soda bicarbonate did not give any relief. The last four days, the pain was constant and accompanied by nausea and vomiting.

Physical examination showed an obese woman, fifty-seven years of age, acutely ill

fingers below the costal margin. A small ventral hernia was present. A flat x-ray of the abdomen showed a large gallbladder clamp within the abdominal cavity.

Operation revealed a large gallbladder clamp, still locked, completely buried and surrounded tightly by adhesions which had to be cut. It was impossible to open the clamp *in situ* before removing it. The hernia was repaired and the patient made an uneventful recovery. To this date, she does not know that she had the gallbladder clamp in her abdomen for two years.

# Selected Book Reviews

THE first edition\* of "Disability Evaluation—Principles of Treatment of Compensable Injuries" came out in 1936. As the author states, "(It) was a venture into a somewhat untrodden textbook field." The author undertook (and successfully) to clarify the subject of physical disability as it pertains to economic loss to labor and industry.

There was a healthy response to this new work and a second edition was published two years later. The book continued to enjoy wide popularity and now the third edition, which has been thoroughly revised with added material through suggestions arising from physicians, lawyers and industrial courts, is offered the profession.

To quote Dr. McBride: "The composite schedule of disability evaluations included in this edition was formulated after a great deal of investigation. Such existing rating schedules as that of the United States Veterans' Administration and other legalized standards were used as a pattern. The percentages and principles of rating disabilities, as cited in this table, are therefore based on medical opinion, supported by legal and statutory experiences. A reasonably definite standard of average ratings is thus presented to provide a ready reference in formulating decisions and opinions as to the evaluation of disability."

There is a new chapter on the responsibility of the doctor as an expert witness. After a chapter on basic surgery, chapters follow on the subjects of workman's compensation laws, standardizing medical evaluation of disability, the procedure of analysis in evaluation of disability, examination of the disabled person, joint stiffness, chapters on ankylosis of the shoulder joint, elbow joint, wrist joint, the hand as a unit, the fingers, the hip joint, the knee joint, ankle joint, and the toe joints, chapters on the disability of fractures, fractures of the clavicle, scapula, humerus, forearm, carpus, metacarpus and phalanges, pelvis, femur, tibia and fibula, the tarsal bones, the industrial back, the trunk, nerve injuries, amputations, head injuries, injuries of the eye, injuries of the ear, burns and hernia.

\* Disability Evaluation—Principles of Treatment of Compensable Injuries. By Earl D. McBride, B.S., M.D., F.A.C.S. Third Edition Revised. Philadelphia, 1942. J. B. Lippincott Company. Price \$9.00.

The book numbers 631 pages and there are 374 illustrations. There is also a bibliography and an ample index.

To all physicians engaged in this type of work this valuable book is seriously recommended.

"The Principles of Anatomy as Seen in the Hand"\*\* appeared originally during the first World War in 1914. It was written, as the author tells us, because the many war injuries that involved the functional use of the hands in civilian life formed at that time an outstanding problem in the passage of discharge from military service. Therefore, "It seemed obvious that no proper assessment of military disablement could be translated into terms of civilian disability unless the functional anatomy of the hand was properly realized. This resulted in a series of lectures as a part of the course of instruction of officers of the R.A.M.S.C. at the Special Military Surgical Hospital, Shepard's Bush." Naturally, this edition was out of print and out of date for many years. Therefore, a new edition was practically rewritten which includes six new chapters and twenty new illustrations.

Written by the Professor of Anatomy, at the University of Manchester, the book is fundamentally and scientifically sound. Added to this a freely flowing style makes a rather dry subject interesting and engaging.

The illustrations are good. There is an unstinted bibliography for those who wish to delve deeper into the subject and the index of subjects is also ample.

In these times every surgeon in civilian practice and, above all, every surgeon in the armed forces, would do well to give this work on the "Anatomy as Seen in the Hand" his serious attention.

The treatment of burns offers debatable aspects. Many years ago the problem was settled by the housewife who rubbed lard on her scalded child. Decades passed and in the laboratory research workers attempted to determine the exact nature of burn "toxemia." There is a wide gulf and lack of adjustment between the two. Dr. Harkins has presented all sides of the question, and in the writing of his monograph† has contributed a great deal. Anyone who reads "The

\* The Principles of Anatomy as Seen in the Hand. By Frederick Wood Jones, D.Sc., F.R.S., F.R.C.S. Second Edition. Baltimore, 1942. The Williams & Wilkins Company. Price \$7.50.

† The Treatment of Burns. By Henry N. Harkins, M.S., M.D., PH.D., F.A.C.S. Springfield, 1942. Charles C. Thomas. Price \$6.50.

"Treatment of Burns" is sure to view the subject from a new and broader viewpoint.

This comprehensive work on burn therapy concerns itself with pathology, chemistry and blood concentration. It deals with primary and secondary shock, the rôle of the adrenals, of fluid loss, of toxins and of bacteria in burns. We learn of the early and late complications in burns, of general and local treatment, of the new discoveries and of recent international developments. Burns disfigure; hence early and late plastic treatments are considered. Special burns, regional burns, electrical and radiation burns, chemical burns, and freezing, as well as war burns and industrial burns are all included in this text.

Today a book of this character is timely and needed. It is well written; the publisher has given us a good book to look at and to hold. It is nicely illustrated, contains a lengthy bibliography and an index of both authors and subjects.

Richard C. Cabot, late Professor of Clinical Medicine, at Harvard University, first published his "Physical Diagnosis"/\* in 1900. Since then twelve editions and many reprintings have come off the press (the twelfth edition was by Cabot and Adams), and now the thirteenth edition is by Dr. Adams. What Doctor of Medicine, graduated during the last forty years, does not know of Cabot's Physical Diagnosis? (It is hard for us to say Cabot and Adams "Physical Diagnosis" by F. Dennette Adams, but, no doubt, in time we will learn.) The writer bought a copy while a medical student about thirty-six years ago. It fascinated him. He has owned and used other editions since then.

Something "new has been added" to each new edition. Medicine does not stand still, and the first "Physical Diagnosis" seems an anemic little thing alongside this new 888-page volume. We do not review this "standard" in order that you make its acquaintance; we are simply telling you that Dr. Adams has revised and brought up to date this old friend. Much new material has been added; many sections and passages have been rewritten and the illustrative material has been modernized by replacing many of the older illustrations with better ones. The publishers write on the jacket that "it will continue to be the first choice of teachers." Perhaps, after all, this is only a mere statement of fact. We are happy this old friend is still with us.

\* Cabot and Adams *Physical Diagnosis*. By F. Dennette Adams, M.D. New Thirteenth Edition. Baltimore, 1942. The Williams & Wilkins Company. Price \$5.00.

# The American Journal of Surgery

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## Editorial

### CONDITIONS ASSOCIATED WITH HYPERTHYROIDISM

IT is important to recognize and to understand correctly the surgical and medical conditions which may be associated with hyperthyroidism in order to evaluate their effect upon the degree of hyperthyroidism or, conversely, the effect of the hyperthyroidism upon these associated conditions. It is equally important to recognize hyperthyroidism which may be present as the primary disease in a patient who consults the surgeon for such conditions as hernia, pathological disorders of the gallbladder, fibroid tumors and other diseases. In rare instances, acute abdominal lesions and certain traumas—as fractures or dislocations—must be treated primarily; but the hyperthyroidism, if present, must be recognized and treated properly during the postoperative period.

Muller<sup>1</sup> reported serious reactions which followed in three patients with unrecognized hyperthyroidism who were operated upon for a tumor of the breast, a dilatation and curettage for a submucous fibroid and for nephrolithiasis.

The occasional development of an acute surgical complication or an acute illness as pneumonia or tonsillitis, in a patient with hyperthyroidism who is undergoing preoperative treatment, demands a display of the best type of judgment. It has long been appreciated by those who have studied this disease that the patient with hyperthyroidism tolerates infections

and traumas—either physical or psychic—badly, and before iodine was employed in the preoperative preparation of these patients, infections and traumas often proved to be fatal factors.

I recall seeing, in consultation, the unfortunate case of a young minister who had had an emergency appendectomy performed because the gastric symptoms of a crisis due to severe hyperthyroidism were thought to be caused by appendicitis. Greene<sup>2</sup> reported a fatal outcome in a patient, following a simple procedure of the injection of varicose veins, which he, personally, had refused to inject because he recognized that the patient was gravely ill with hyperthyroidism. I remember a fatality due to acute tonsillitis which developed in a patient who was being prepared for operation in the pre-iodine days, also a patient who nearly died from the reaction which followed a Colles's fracture sustained while the patient was undergoing preoperative preparation, and an equally severe crisis which developed in a patient whose home was struck by lightning.

Hyperthyroidism must always be recognized, if it should be present, before traumatizing a patient with any type of operation for an associated surgical condition which can be postponed until the hyperthyroidism is under control by proper treatment.

Gallbladder and stomach lesions, tumor of the breast, hernias (except those which are strangulated), or fibroids causing excessive loss of blood are often associated with hyperthyroidism but we believe the hyperthyroidism should have primary consideration, if it is at all possible to postpone the surgical treatment of the other conditions.

The case of Mrs. B. illustrated this point very well, for she required three major operations to correct her difficulties. She had primary hyperthyroidism of a moderately severe degree, frequent attacks of severe gallstone colic and had lost excessive amounts of blood at her menstrual period from a large uterine fibroid. A thyroidectomy was performed safely after a period of adequate preparation, a few months later the gallbladder was removed and a hysterectomy was performed two months after the cholecystectomy. Had either of these apparently urgent conditions been operated upon first, and had the hyperthyroidism not been recognized, she might have developed uncontrollable hyperthyroidism.

Diabetes and cardiovascular disease are often associated with hydrothyroidism; less frequently we encounter pulmonary tuberculosis, pregnancy and pernicious anemia. Transient glycosuria is often present with hyperthyroidism and should be recognized and differentiated from true diabetes. Cattell<sup>2</sup> found that true diabetes was present in 1.5 per cent of his hyperthyroid patients. The diabetic patient, of course, is a very substandard person but, with the control of the disease by modern methods in the preoperative preparation of the patient and by the use of conservative operations, the diabetic patient can be treated for hyperthyroidism with a much better degree of safety than that which existed previously.

The cardiac complications of hyperthyroidism are seen in patients who have independent or primary heart disease and also in those showing disturbances in heart rate, rhythm and with degrees of decompensation with edema which are due

entirely to the hyperthyroidism. Lahey has very properly classified these patients as thyrocardiacs. Many of these bad risk goiter patients may be operated upon safely; sometimes, however, after prolonged and adequate preoperative treatment which may require many weeks, the miraculous improvement which often follows is indeed surprising. The postoperative results, however, in patients who suffer with severe degrees of associated primary cardiovascular disease are likely to be disappointing.

Pregnancy often complicates hyperthyroidism but has not proved to be a dangerous or very troublesome complication. In our experience, we have had no miscarriages follow thyroidectomy.

Pulmonary tuberculosis is a dangerous complication. Active pulmonary tuberculosis has an aggravating effect upon hyperthyroidism and the tuberculosis is rendered more active and dangerous by the hyperthyroidism. It is also believed that acute hyperthyroidism will reactivate a quiescent pulmonary lesion and for these reasons it is thought best to control the hyperthyroidism by operation, although the outlook in many of these cases is not favorable.

Patients with pernicious anemia respond very well to thyroidectomy if the primary anemia receives proper and adequate treatment.

The presence of hyperthyroidism must always be recognized and our primary interest should be in its control. It is extremely important, however, to recognize and treat the conditions which may be associated with it, if the patient is to be cured of the hyperthyroidism with safety.

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DONALD GUTHRIE, M.D.

# Original Articles

## MANAGEMENT OF MAJOR COMPOUND FRACTURES OF THE SKULL VAULT

JOHN T. B. CARMODY,\* M.D.

Neurosurgeon, Worcester City and Worcester Memorial Hospitals

WORCESTER, MASSACHUSETTS

THIS study is composed of a group of compound fractures of the skull vault taken from a series of 1,411 hospital admissions for head injuries. There have been forty-two such cases. Actually, they form a small percentage—approximately 3 per cent—of the total and are, therefore, the type of case that is not seen frequently except in the larger industrial and more populated areas. With the possible exception of the bursting or stellate fractures of the skull, this group includes the severest types of craniocerebral injury. Although the incidence is slight in the average community, the automobile has extended the distribution of these injuries, and as a result, every surgeon will be confronted occasionally with the problem of their treatment. It is primarily with this point in mind that this paper is being presented. It is not an attempt to advocate or expound major changes in the neurosurgical approach, but rather it is offered as an aid to those who either must or insist on accepting the responsibility for their management.

In defining a compound fracture of the skull vault, one is aware that the range of severity may be great. The injury may consist of a tiny scalp laceration overlying a small crack in the outer table of the skull with no directly associated brain damage. It may on the other hand, comprise a crushing injury with multiple depressed comminuted fragments complicated by

herniation of the cerebral tissue. Obviously, the method and extent of treatment differ depending upon the degree of involvement. It is the handling of these latter cases that demands the rigorous adherence to well founded principles of treatment.

In a recent paper, Coleman emphasizes the point that the neurosurgical principles of technic were formulated by Harvey Cushing in the treatment of such cases during the first World War. Prior to that time the technical management varied with the surgeon and no logical course was persistently pursued. The mortality rate was always high and was consistently related to the incidence of infection. DeMartel and Vincent, in reviewing their own experiences, speak of death in as high as 60 per cent of the cases, and they blame these excessive figures on infection. They, too, have noted a marked lowering in this percentage in dealing with more recent properly treated series. Fundamentally, the technic of treatment is that of total surgical débridement of the injured tissues. However, as might be supposed, there has been a wide variation concerning the requirements for fulfillment of total débridement. Formerly, with respect to the skull, it consisted of extensive block removal of the injured area; the procedure being performed by means of burr holes connected by the use of the DeVilbiss rongeur. The accompanying diagram illustrates this method of technic. (Fig. 1.)

\*Dr. Carmody is now a Lieutenant Commander on active duty in the Medical Corps, U.S.N.R.

The dura was widely resected and the damaged cerebral tissue was removed by suction and irrigation. Today the primary

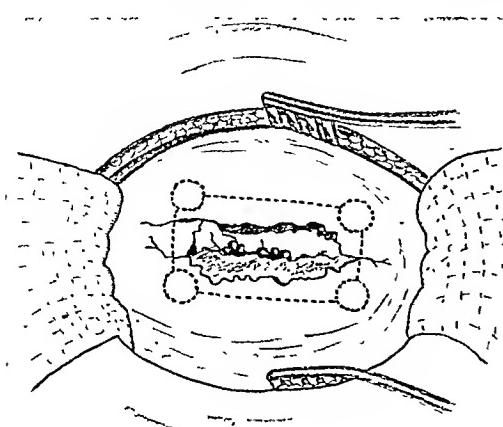


FIG. 1. Usual method of block removal of the skull.

principle of débridement is carried out similarly, but the extensiveness of actual tissue removal should be less radical. In discussing this present series I shall attempt to indicate my reasons for advocating a more conservative approach.

A second important factor which experience has derived from the first World War and since is the element of time. The decision as to when to operate demanded then, as today, the most careful consideration. The optimum time was thought to be within twenty-four hours, as observation showed in the wounded a marked increase in the incidence of infection beyond that period, no matter how adequately the surgical procedure was performed. Undoubtedly, transportation difficulties accounted for a large toll in cases of this sort. Such major surgical procedures could not be taken care of satisfactorily in temporary stations along the front. As a result, many of this type would not arrive at the proper bases until it was too late to accomplish anything worth while. DeMartel pointed out that often as long an interval as two weeks was spent in the transit from the initial station. Now, such delays should be eliminated largely. This holds true whether the case in question is a crushed skull from an automobile accident along a country

highway, or a similar injury occurring in the line of attack of an advancing mechanized unit. There continues to be considerable controversy concerning the ability of severely injured head cases to withstand the strain of moving. Some are of the opinion that more can be gained by treating these patients in the nearest possible station from the scene of the accident. This point of view is based upon fallacious reasoning and it is a well established fact that these severe cases stand transportation much better preoperatively than they do soon after operation. Especially is this so provided supportive methods for combatting shock have been utilized as a preliminary step.

There is a distinct parallel between the severe head injuries of civil life and many of those occurring in modern war. Penetrating wounds of the brain with retained foreign bodies must be frequent but the impression is gathered from the available literature that the crushing injury without retention of missiles is also prevalent. Certainly this is true with respect to the civilian population suffering from air bombings. Consequently, the management of these cases should not vary and the principles involving time, transportation and operative treatment should help reduce the morbidity and mortality rates.

#### TECHNIC

Much has been written concerning the handling of these cases, but the details which may be significant are frequently taken for granted or ignored. Therefore, the details are listed as completely as possible and for clarification, the technic of management is divided into four stages; preparatory, preoperative, operative and postoperative. It must be emphasized that all cases need not progress in this orderly manner.

*I. Preparatory Phase.* If the patient is within a reasonable distance of a properly equipped base or hospital, he should be transported immediately to that place. If the distance is considerable and the

general condition (the degree of shock being the chief determining factor) is such that the time spent in transit might cause jeopardy, he should be brought to the nearest available point where preliminary supportive procedures may be carried out. In either case, these supportive measures will be the same. Most of these patients will either be in or on the verge of traumatic shock. The color and appearance of the skin is probably the most reliable index although the pulse and blood pressure may give irrefutable evidence of the development of this condition. With the onset of collapse, the true character of the pulse and blood pressure may be clouded by complicating increasing intracranial pressure or dehydration, whereas the skin by its pale appearance and clammy feel will be a more accurate gauge. Fluids given intravenously or blood transfusions, if there has been any severe loss of blood, are the best and quickest counteracting force. Fluids should be given immediately even though transfusion is warranted, in order to span the interval necessary for details such as blood grouping. With respect to the type of fluid there is not much choice. Glucose in concentrations of 25 per cent and in amounts of 200 cc. will offer most chance of immediate effect. Drugs such as coramine and caffeine are helpful and may give an added impetus in preventing collapse. Simple mechanical means should not be ignored and warm blankets or hot water bottles properly placed will aid greatly.

During this period which is entirely one of preparation for surgical intervention, attention is at the same time given to the head wound. When the general appearance of the wound confirms the diagnosis, handling or palpation by the gloved finger is not warranted. Such examination is for the less obvious and more simple types of injuries, as in determining the presence of a crack underlying a scalp laceration. If palpation is necessary, it should be done by one person only, preferably the surgeon. It is my firm opinion that skull fragments

or other débris, no matter how superficially they may appear to lie, should never be removed at this time. A partially



FIG. 2. Shield protecting right frontal bone defect.

ruptured vessel, for example, may remain blocked off by either indirect or direct pressure from a depressed fragment. If such a fragment is freed or lifted out, uncontrollable hemorrhage may follow. Dry sterile dressings applied to the wound and held in position by a sterile towel make a most satisfactory temporary dressing under all circumstances.

Severe irreparable injuries will usually succumb within a few hours and their course will be characterized by a progressively downward trend. If the patient has been placed in a preliminary station and there have been no indications of improvement, there is little point in contemplating removal to a more fully equipped base. There are of course exceptions, as in those cases complicated by the acute hematoma group. This latter group is more often seen, however, in the other general classes of head injuries. Davidoff and others agree that during this preparatory period the answer will solve itself usually in a period of ten to twelve hours. This statement has been borne out in this present series. The

greater percentage of the nonoperative deaths occurred within twelve hours after hospital admission.



FIG. 3. Gunshot wound of the head with retained bullet.

Another beneficial step which may be included under the heading of support is that of lumbar puncture. Generally speaking, it is of less value in this sort of injury. Many of these compound vault fractures will decompress themselves either by extrusion of damaged brain tissue or by the loss of cerebral spinal fluid. As a matter of fact, this is probably the chief reason, together with the localized nature of the brain damage, why some of these severely injured patients are temporarily conscious and in relatively good condition. When the fracture is such that extrusion or drainage is prevented, the intracranial pressure will certainly increase. The extent and rapidity of the increase may depend on the development of an acute hematoma. Spinal drainage will often help to counteract fatal cerebral compressions until surgical intervention can be performed.

*II. Preoperative Phase.* The second phase of therapy will follow when there is evidence that the patient's general condition has shown improvement. It should consist of the actual details of preparation for surgical intervention. It will be necessary to handle the patient at this time, but all manipulation should be carried out as carefully as possible, and it may be advantageous to remove the clothing by cutting it. A general examination is next

performed. Fractures of the long bones, cervical vertebrae and chest injuries are frequent complications which may be missed due to focusing the attention on the head injury alone. A complete neurological examination cannot be done always in an adequate manner, but gross abnormalities are easily detected and are of definite value in the consideration of when to intervene. From the neurological point of view there is less information to be gained by minute observation in these cases than in other classes of head injuries. In the latter types, the question of whether operative intervention should be performed, or whether the patient should be treated by conservative means may hinge on the progression of abnormal neurological signs. By far the most important value gained from an adequate analysis of the neurological status of the patient concerns the intracranial pressure. If repeated examination shows increasing gross discrepancies in the pupils or reflexes, or the development of convulsions or paralysis, one may assume usually that the intracranial pressure is beyond control of ordinary methods; and immediate operation, whether there has been a noted general improvement from the preliminary support or not, may be considered the only hopeful procedure.

The question of medication is a major problem. Suffice it is to say that all sedation should be avoided whenever possible. Patients with head injuries are notoriously restless, and when the restlessness is attributable to increased intracranial pressure, it may be controlled by a combination of the above methods. However, it is often the result of brain damage and it is then that medication of the proper type must be employed. When the patient is unconscious and shows but a moderate degree of restlessness, good nursing care alone will take care of the situation. When the restlessness proceeds beyond this stage, medication cannot be avoided. Paraldehyde in doses of 2 to 4 dr. by rectum or mouth is a most satisfactory drug. If this

fails to obviate the situation, sodium luminal may be used in dosages of 3 gr. by injection. Should the restlessness continue

concerning their importance when the fracture is severely comminuted as is true in the majority of these cases. A pre-



FIG. 4. Herniating lacerated brain tissue complicating a right parietal compound fracture.

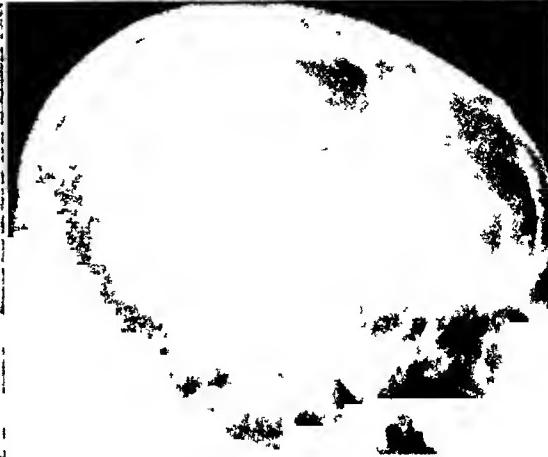


FIG. 5. New bone formation two years post-operatively.

to be unabated, the condition may be uncontrollable by the usual simple drugs. Although morphine is contraindicated generally, due to its known aggravating influence on the intracranial pressure and its depressing effect on the respiratory center, such stronger medication appears to be absolutely necessary in some instances. Repeated dosages of paraaldehyde in conjunction with small dosages of morphine,  $\frac{1}{10}$  to  $\frac{1}{2}$  gr. have given excellent results without evidence of any dilatorious effects. Tetanus antitoxin of 1500 units should be given after the proper precautions against sensitivity have been taken. Chemotherapy must be started at once. At this point it may be assumed that the supportive measures have achieved the desired purpose, and if the optimum time for surgical intervention has been reached, any further delay will be harmful.

En route to surgery x-ray examination may be undertaken. Portable films are usually worthless, but a good lateral and postero-anterior view can be obtained with most equipment without removing the patient from the truck. Here again, the value and necessity of preoperative skull plates have been the subject of much discussion. There is no question in my mind

operative knowledge of the extent and number of the fragments is an advantage. In gunshot wounds or when other types of foreign bodies are suspected of being retained, x-ray examination is mandatory.

Before operation the head is shaved under sterile precautions as completely as possible. The scalp is then washed with green soap and rinsed with alcohol. When an anesthetic is necessary, it has to be administered before attempting to prepare the head because of lack of co-operation on the part of the patient.

Concerning the anesthetic itself, the same principles hold true as with respect to medication. A general anesthetic is avoided whenever possible and as most of the patients are unconscious, the decision is made automatically. When anesthesia must be used, local  $\frac{1}{2}$  per cent novocain with 6 drops of adrenalin per ounce is the first choice. It is most satisfactory in conscious patients who will co-operate. For many, however, it is a severe ordeal and a tremendous strain. In the semicomatose patients, local anesthesia is not ideal. The patients do not experience pain but often cannot maintain a fixed position and become difficult to control. Since they are clouded mentally, reassurance by the surgeon has no effect,

and since a general anesthesia must be resorted to finally, time is saved by using it from the beginning. Of the general

scalp wound is comparatively small in relation to the skull involvement, or the depressed area is at some distance from the



FIG. 6. Penetrating wound of the right front skull.



FIG. 7. Postoperative skull defect.  
Same case as Figure 6.

anesthetics, drop ether is the best. Usually only a small amount is necessary and a competent anesthetist is able to carry the patient on a light level. Ether increases the intracranial pressure, but this fact although a disadvantage, does not contraindicate its use. Intravenous pentothol is satisfactory, but must be used with care due to the depressing effect upon the respiratory center. I have preferred the use of this drug in head cases demanding less extensive procedures.

*III. Operative Stage.* The head and neck are supported by a small pillow in position for the correct approach. The scalp is prepared with any of the several well known antiseptic solutions. One is probably as good as the next, but cleansing with ether followed by iodine and then alcohol was the procedure used in this series. Strong antiseptics should not be poured directly into a gaping wound due to the possibility of causing further tissue destruction. The operative field is then draped carefully. The scalp incision demands thought and will vary with each particular case. When the laceration is extensive or directly overlies the point of fracture, the approach is made there best, even though extension of the incision may be required. On the other hand, when the

scalp wound, it is better to turn down a curved flap from above. Also in frontal lesions where greater exposure is needed, a flap incision above the hair line has a more desirable cosmetic effect. Occasionally, cases of this classification, but not of such major proportions, will have undergone some surgical intervention several days before being transferred. This intervention is characterized most often by the suturing of the scalp laceration. When such an incident has taken place, an interval of time must be allowed to elapse. During this interval, intensive chemotherapy is instigated and the interval itself must be of sufficient length for complete healing before the final procedure is carried out.

A curved incision above the laceration is demanded as a further precaution against infection. In gunshot wounds which have been fired from a short distance, and the wounds which have resulted in destruction of extensive area of the scalp, or which require wide scalp débridement are best handled by the tripod incision as advocated by Cushing and others to allow for the proper closure. At any event, following sufficient exposure, the skin edges are held in position by self retaining rake retractors, and thus fewer scalp clamps are required. Any means which can be used to lessen

further disturbances of the blood supply should be fully utilized. Complete débridement of the skin edges must be accom-

either by underfracture of the inner table with overlapping of the outer table or by interlocking at the apex of the depression.



FIG. 8. Extensive right frontal skull fracture.

plished before proceeding further, and the contaminated instruments should be discarded. Ideally, the surgeon would prefer to attack his problem from the center of the involved area, working toward the periphery as the destroyed and potentially infected tissue is removed in a concentric manner. This cannot be accomplished in most instances because ordinarily the first presenting tissue is the herniating portion of the brain. This mass is always edematous, hemorrhagic and in various degrees of necrosis, depending upon the factors of time and the disturbance in the blood supply. This tissue is removed readily by suction. Considerable bleeding may occur, but can be controlled by packing with cotton pledges, muscle packs, and by clipping the larger vessels. After removal of this mass, the extent of the fractured area is exposed fairly completely.

It is to be noted that very frequently the fracture will be a much more extensive affair than one would have supposed. This will be found to be true particularly with respect to the inner skull table. The bony edges are encountered and these are removed by elevating the fragments and then lifting them out. Occasionally, the depressed pieces are interlocked and the entire fractured portion is immobilized



FIG. 9. Slight bone regeneration is present.  
Same case as Figure 8.

When this situation presents itself, it is necessary to remove a small amount of bone at the edge of the fractured site in order to place the elevator in a workable position. All fragments which are detached definitely and comminuted or in which the blood supply has been affected should be removed. Following this step the fractured edges of the intact skull are trimmed by means of the rongeur. Major bleeding may occur from the deploic vessels, but it can be controlled by simple packing or by the use of bone wax. Bone wax should be used sparingly due to the fact that infection might be encouraged by blocking off these spaces. At times a large bony area such as the squamous portion of the temporal bone with linear fracture lines running well into the base may be involved. If this entire area was removed, it would leave a tremendous defect; and since the blood supply is not embarrassed greatly, the fragmented mass may be elevated or pried back into position and the edges simply freshened. With removal of the fragments, extra dural clots or even large hematomas may be encountered. The suction will remove these and expose adequately the lacerated dura beneath. The contaminated and frayed edges are removed completely and silk or

cotton retracting sutures are placed strategically in order to expose the cortex sufficiently. Further extension of the expo-



FIG. 10. Bone defect following débridement of left occipital fracture.



FIG. 11. Postoperative defect following removal of subdural hematoma. Same case as Figure 10.

sure may be justified by incising the dura for the purpose of correctly evaluating the amount of brain damage. The cortex will range in color with relationship to the severity of the injury from a pink injection to the deep reddish purple of an over-ripe plum. The landmarks may be beyond recognition, but a gradual line of demarcation from normal to involved brain can be noted as the color fades from the center of destruction to the periphery. The differentiation between viable and destroyed tissue may not be determined by color alone. Destroyed cerebral tissue is friable and can be removed by a suction of moderate force with ease. It is essential that débridement be complete, although as little viable cerebral tissue as possible should be removed. Especially is this true in the localized functional regions of the parietal and temporal lobes, particularly areas 4 and 6 bilaterally, and 39 through 42 on the speech side. Therefore, the surgeon's judgment must be guided by the factors of viability, location with reference to the possibility of future neurological sequelae and potential infection. Fragments of foreign bodies embedded deeply present a more serious problem and are major threats with respect to infection. Retained foreign

bodies are often the focus when fatal infection follows. The relative location and number are determined by the x-ray, but

actual contact may require an intensive search. The tract of entry is the initial landmark and exploration by suction along this tract is the most satisfactory method. It is here that severe hemorrhage is likely to occur or the complication of rupturing into a ventricle. In gunshot wounds the foreign body may penetrate more closely to another part of the skull surface and in such cases it is preferable to make the approach at the nearest point to that body.

There has been some controversy concerning the use or irrigation in these potentially infected wounds. Coleman and others who have had much experience in the treatment of these cases advocate strongly the copious use of fluids, either saline or Ringer's solution, as an irrigating substance. On the other hand, Munro is of the opinion that the use of irrigation is contraindicated. Smaller fragments and clots will be washed out readily but this can be accomplished just as easily by débridement and with less danger of the spread of organisms. Also, in order to fulfil the purpose of irrigation, the solution must be used with force, which in itself may insult further previously traumatized brain and drive contaminated fluid into clean meningeal spaces. Possibly there is

greater satisfaction in viewing an irrigated cerebral wound with its cleaner general appearance as compared with a similar one which has been débrided solely by the use of suction and cautery, but needless to say, this does not hold that the former has less chance of becoming infected. At any event, what advantages irrigation may offer appear to be inconclusive, and on this basis the patients in this series were treated entirely without its use.

Thorough débridement of the brain will result frequently in a gaping defect with blood welling quickly from its depths, and reflooding as rapidly as it can be removed. Larger vessels are located with the aid of the suction and are controlled by the cautery or clips. However, the general ooze from many tiny bleeders cannot be arrested by these means. Pieces of sterile muscle, chewed up a bit by the scissors, and cottonoid packing placed with slight but firm pressure are valuable adjuncts for hemostasis. Seemingly large cavities will tend to close themselves or gradually reduce in size as such packing is removed slowly. When all bleeding points have been stopped completely, closure of the wound is undertaken. In this type of case it is not likely nor is it desirable that the dura be closed tightly, but as great an extent of the dural edges as is possible without tension should be approximated with interrupted silk or cotton sutures. A dural defect may be left open in most regions. However, with involvement of the frontal bone when there has been an extension into the paranasal sinuses even though that extension is by a single linear crack, the dural defects in that region must be repaired. Muscle or fascial grafts are quite satisfactory, and if placed properly, they will prevent a spinal fluid leak. Most agree that a spinal fluid leak into the sinuses is an unfortunate complication and results in a high incidence of postoperative infection. The skull defect is walled off for the interval required in closing the scalp and the aponeurosis and skin are closed tightly with interrupted sutures in the manner of the usual bone

flap. The wound is closed without drainage. Dry sterile dressings padding the operative field and held in position by means of an



FIG. 12. Right front compound depressed fracture.

Ace bandage are applied. The Ace bandage covering the entire head is an excellent way of immobilizing the dressing and preventing it from slipping; furthermore, it can be regulated for any required amount of pressure. An important point which is occasionally overlooked is the protection of the ears against the mastoid processes. Compression against these bony prominences may result in sloughing of the soft tissues. Supportive measures such as intravenous fluid or blood might have been carried on during the operation. If not, continued support is next given, depending upon the systemic need. When moved from the operating table, the patient is placed with his head at the foot of the bed, thus allowing greater convenience and less handling when the dressing is to be examined.

*IV. Postoperative Phase.* The final stage has been reached and the patient's future course will depend upon the prevention or control of the immediate complications which are bound to occur. The most serious is that of an increase in the intracranial pressure. Associated brain damage directly related to the initial injury probably is the most important single cause. Methods of control are no different than those described in the preoperative stages, and consist of lumbar puncture, intravenous

hypertonic solutions and the judicious use of fluids. The spinal pressure should be recorded and the fluid withdrawn slowly to

recorded which will offer the surgeon a summary of the postoperative course at a single glance. An analysis of the progres-

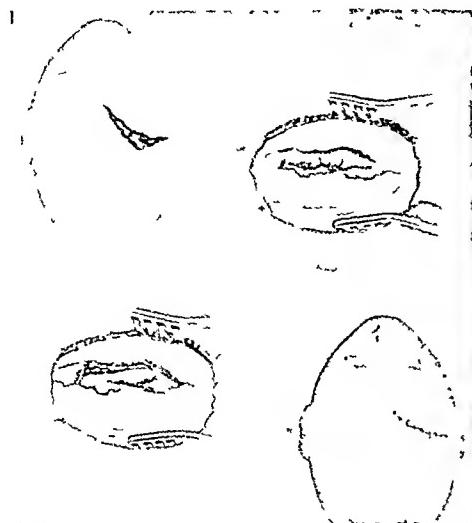


FIG. 13. Various operative steps revealing the extent and character of the fracture. Same case as Figure 12.

produce a normal intracranial level. Dehydration may be a dangerous adjunct. In some instances in spite of attempted control, the intracranial pressure will continue to increase, and when associated with a sharp rise in temperature, a poor prognosis is to be expected. Tapping the ventricular system directly through the operative wound is a procedure which may offer some hope when the situation appears uncontrollable, but certainly it should not be considered as a routine or frequent step. Careful observation from the neurological point of view is a necessity. The development of lateralizing signs in conjunction with an increase in the intracranial pressure is evidence warranting further intervention. One case in this series emphasizes well this particular point.

The vital signs warrant detailed observation. The temperature, pulse, respirations and blood pressure should be followed at regular periods. The routine that has been employed in these cases calls for the charting, not listing, of the signs every fifteen minutes for the first hour, and then every one-half hour depending upon the patient's condition. Thus, a graphic presentation is



FIG. 14. Postoperative defect with some bone regeneration present. Same case as Figures 12 and 13.

sion of these vital signs is a subject of sufficient importance for a separate study. Woodhall and several others have written papers dealing entirely with this matter.

Postoperative medication follows no different pattern from that noted under the preparatory phase of treatment. The drugs are the same and they should be avoided whenever possible. Again, good nursing care is a primary requisite, and in my opinion, has more favorable effect on restlessness than repeated sedation. The intelligent combination of both is the ideal choice.

No presentation in the field of traumatic surgery can be complete without a discussion of chemotherapy. In many instances, the sulfa-derivatives have fulfilled a long anticipated hope in combatting infection. Whether this hope has reached unwarranted levels in other circumstances is a moot question. Certainly, chemotherapy should not supercede or allow any weakness in the thoroughness of surgical technic. Rather, it should assume the lead in a supporting capacity, essentially a prop with both moral and specific attributes. In the consideration of all our compound frac-

tures, most were treated with some form of the drug, beginning with sulfanilamide and progressing with each suspected ad-

ditional powder followed by the parenteral use of sulfadiazine seems to be the best combination now in use.



FIG. 15. Compound fracture involving frontal sinuses.



FIG. 16. Postoperative film. Same case as Figure 15.

vancement. Sulfadiazine, at the present writing, is supposed to have attained a greater value than the others and has been used, but due to its unavailability, not in this series. The application of the drug varies with the case. It has been our custom to give some form in a prophylactic measure. First, sulfanilamide, more recently sulfathiazol, and now sulfadiazine, in dosages of 60 to 80 gr. initially, followed by 15 gr. every six hours for one week. There is no evidence to substantiate the fact that these derivatives have been influential in a preventative capacity. Local application of sulfanilamide in the powder form has been advocated, and it is believed that cerebral tissues tolerate well its direct contact. In evaluating the rôle of chemotherapy, one is aware that in established infection of particular types, it is a distinct asset approaching specific qualifications. When viewed from the aspect of prophylaxis, its status continues to be uncertain. However, until proved otherwise, the best opinion indicates that it should be used in this way. Of the various forms, sulfadiazine is thought to offer the most for prophylactic purposes. Dusting the wound lightly with sulfanilamide

immediate continued rise in the temperature postoperatively is the gravest single prognostic sign. When levels of 104° to 105°F. are reached within forty-eight hours, it usually indicates severe brain damage and the outcome may be considered very doubtful. The first five post-operative days constitute the critical period, and if this type of case survives to the fifth day, the prognosis for life is usually favorable. This assumption of course deals with the effect of brain damage alone and is tempered by the development of any complication. If two weeks have elapsed before any evidence of a fatal infection, the threat of direct brain trauma will have subsided.

It makes little difference when the sutures are removed. If the incision is noticeable, a better cosmetic result will be afforded if they are taken out early, between the third and fifth day. If the convalescence has been uneventful and the period of unconsciousness has not extended beyond three to four days, most patients may be out of bed in two weeks from the day of operation. Prior to discharge from the hospital, X-rays of the skull must be taken. These films are to determine first, whether all fragments or foreign bodies

have been removed successfully, and secondly, as an aid in performing any later operative procedure.



FIG. 17. Compound depressed fracture of right frontal region.

could be prevented by less extensive removal of bone at the time of the initial operation. If the rongeur is used to trim the



FIG. 18. Postoperative defect. Same case as Figure 17.

Symptoms arising from extensive removal of sections of the skull are present in many cases. The severity of these symptoms is related often to the size of the defect and is characterized by a feeling of insecurity associated with disturbances in equilibrium. Also, headaches and "sensations of fluid flowing back and forth inside the head" may be severe enough to cause complete disability. Furthermore, pulsations are noticeable to the patient when the defect is of any size and may be aggravated when the position of the head is changed suddenly. As a result of this postoperative symptomatology, extensive studies have been carried out by many in the hope of alleviating these complaints by further surgical means. Various types of fixed metal plates covering the bony defect such as silver and light steel alloys have been recommended, but they have proved to be of questionable value. Attempts with celluloid have been more successful, but by far the best result has been obtained from direct bone grafting. Turning down a portion of the outer skull table adjacent to the defect in the manner of any pedicle type graft as originated by Konig and Mueller, was the repair used by Bagley, and in general appears to be the most worth while procedure. It is my opinion that many of these cases of large defect

involved bone margins carrying the resection back far enough to insure adequate blood supply, much bone can be saved in comparison with the usual block removal. The main argument against this method of approach is the feeling that anything less than a radical block resection encourages infection. This assumption has not been true in these cases although this presented series is not a large one, and there has been no postoperative infection attributable to this source. Also, in the future, if the prophylactic qualifications of chemotherapy assume a concrete form it will give an added impetus to the conservative trend. Especially in children, regeneration may sometimes occur thus requiring no further intervention. Adults are less fortunate and when the defect is of major portions or the symptomatology marked, further repair must be considered. A head support covering the involved area is recommended and the type shown in the accompanying illustration made of a light plastic material has been used with good results. (Fig. 2.) Such a guard offers some definite advantages. Protection is afforded and perhaps more important, the symptoms of insecurity are decidedly less apparent. Children should wear such a support for approximately one year, and if by that time there has been no evidence of regener-

ation, bone grafting should be contemplated. In adults the length of time is problematical, but it can be assumed that the most sizable defects will have to undergo repair.

Other postoperative symptomatology will depend on the degree of neurological involvement. Individuals with major cerebral defects are apt to have sequelae varying in severity from headaches to major convulsions. Those whose brain damage has been less extensive or localized to the more silent regions of the brain may be relatively free. This has been particularly true in children, the majority of whom have had no persistent complaints. Further treatment is guided by the severity of these neurological manifestations.

#### CASE SUMMARIES

There are 42 cases comprising this study based on 1,411 hospital admissions over the period 1937 to 1940. Of this number, nineteen did not undergo operative intervention. The majority of these nonoperative cases died shortly after admission. The mortality rate was 100 per cent. There were two cases in this nonoperative group that survived relatively long hospital courses, one of three days, and the other of six days' duration.

The first case (J. N., age sixty-six) was the victim of an explosion. She received a left frontal compound fracture with complications of second and third degree burns. The patient failed to rally with supportive measures and although she gave no indication that her prognosis would be anything but hopeless, she lasted a longer interval than was thought to be possible.

The second case (I. C., age thirty-four) fell three stories landing on a concrete pavement. The vault injury was a compound fracture of the right parietal area with laceration and herniation of the brain. There were also extensive fractures through the base with drainage of blood and spinal fluid from the ears bilaterally. The patient rallied somewhat with supportive treatment but the temperature continued to range from 102° to 104°F. On the third day, evidence of pneumonia developed and he

finally succumbed on the sixth hospital day. Probably this case would not have survived an operative procedure, but in retrospect the hospital course was longer than was justified without intervention.

The remaining cases, twenty-three in number, underwent surgical intervention in accordance with the technic described above. There were three postoperative deaths with a mortality rate of 13 per cent. Of the twenty patients who survived, severe acute complications occurred in three cases, two of which were hematomas and one an infection. Briefly, the cases in which death occurred were as follows:

**CASE I.** (J. V., age fourteen). The patient was struck by an automobile. The injury involved the left parietal area. There was a right hemiparesis. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the left vault with laceration and herniation of the brain, and a compound fracture of the left base. The patient was in profound shock. He rallied with supportive measures. A total débridement was performed approximately twelve hours after admission, but he failed to continue satisfactorily and succumbed on the third postoperative day. There was no infection present.

**CASE II.** (J. P., age sixty.) The patient was injured in an automobile accident. The vault injury involved the high frontal region of the skull. The patient was in profound traumatic shock. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the vault with laceration and herniation of the brain and fracture of the left femur. Improvement was noted after the administration of supportive measures. Surgical intervention was performed ten hours after admission. Postoperatively the patient's general condition failed to hold a satisfactory course. He became worse progressively, his course was characterized by cardiorespiratory failure, and he died on the sixth postoperative day.

**CASE III.** (J. E., age twenty-four.) On May 11, 1939 this patient was shot twice in the head at close range. On admission, he was found to be irrational and extremely restless. The pulse was 54, the blood pressure 104/68 and the respirations rapid but regular. The

diagnosis was a gunshot wound of the head with a compound, comminuted depressed fracture of the skull, right parietal with retained foreign bodies. There was some gradual response to supportive treatment. X-ray examination revealed a retained bullet in the midbrain region. Surgical intervention was carried out with total débridement approximately eighteen hours after admission. Several unsuccessful attempts were made to remove the deeply embedded bullet shown in Figure 3. It was found to have penetrated closely to the right lateral ventricle. Accordingly, when it was not located easily, further attempts were discontinued because of the danger of rupturing the ventricle wall. It was considered better judgment to attempt removal at a second sitting from a temporal approach. A small drain was inserted in the line of closure. Post-operatively, chemotherapy was pushed intensively, and on the fourth postoperative day the temperature and pulse were normal and the patient had regained consciousness. On the seventh day postoperatively there was a full blown meningitis. The temperature had risen to 105°F. and the spinal fluid showed 6,000 white cells, with a positive culture for non-hemolytic streptococci. From this point progress grew rapidly worse and the patient succumbed on the twelfth postoperative day with the temperature climbing to 108°F.

Postmortem examination revealed the bullet to have lodged in the middle fossa behind the Gasserian ganglion. The tract showed that the bullet had barely missed the ventricular wall, having penetrated the subarachnoid space but not the dura. There was an extensive meningitis radiating from this focus involving the entire basilar surface of the brain. This case emphasizes the necessity of complete surgical débridement including the removal of foreign bodies. Chemotherapy under the circumstances was useless. The patient's postoperative course was such as to have led me to believe that he would have survived had the bullet been removed and in retrospect it would have been better judgment to have made further attempts in spite of the proximity to the ventricular wall.

The following cases are presented in a summary form. They have been selected from the survival group in an attempt to illustrate particular points emphasized in the discussion.

**CASE IV.** (S. P., age eight.) The patient was struck by a truck March 29, 1938. He was moved immediately to a local hospital where the diagnosis was noted as cerebral concussion, compound comminuted depressed fracture of the right parietal skull vault, laceration with herniation of the brain and severe traumatic shock. He responded to supportive treatment and eighteen hours after his injury he was transferred twenty-five miles for operation. On admission he was found to be stuporous; the pulse was 100, the blood pressure 100/58 and the respirations were regular. There was some left paresis associated with increased peripheral reflexia. Figure 4 illustrates the region of the injury showing the herniating brain extruding from the wound. Total débridement was performed soon after admission. The patient's postoperative course progressed satisfactorily without any major complications. He was discharged on April 27, 1938. There was at that time a slight left hemiparesis involving the lower face as well as the extremities.

Follow-up record indicated that on October 16, 1938 this patient had no subjective complaints. He wore a supportive shield over the bony defect without difficulty. He was said to be a behavior problem and was getting into trouble constantly. Examination revealed a slight residual left central facial paralysis with some exaggeration of the left peripheral reflexes. Since then he has become less of a behavior problem and has done well in school. The physical findings remain about the same and there is no motor weakness. The post-operative defect has filled in markedly. Figure 5 is an illustration of a film taken two years postoperatively. New bone formation is present and the bony defect is shown to be receding. This case is an example of the advantage in transporting patients to an adequate base for proper treatment. Also it shows the ability of bone regeneration in children. A plastic procedure will not be necessary in this particular case.

**CASE V.** (J. G., age forty-two.) On October 13, 1939, the patient, an iron worker, was struck on the head by a wrench which was dropped a distance of sixty to seventy feet. The handle penetrated through his cap and became embedded at a depth of three inches. The wrench was pulled out by a fellow-workman who noticed a sudden gush of blood. On admission to the hospital the patient was

irrational, extremely restless and had three generalized convulsions. Examination of the head revealed a laceration approximately one and one-half inches in extent in the right frontal region almost to the midline. The wound was oozing slightly. No adequate neurological examination could be performed due to the patient's condition. Immediate operation was considered the only procedure of choice. En route to the surgery, one lateral film (Fig. 6) was taken without removing the patient from the truck. It revealed the extent of the depressed comminuted fragments, and showed that there were no deeply retained foreign bodies. On exploration, a large hematoma involving the subdural space and extending into the right frontal lobe was evacuated. The tract of the wrench was found to have been oblique in direction, penetrating the falx and entering the left frontal lobe. One fragment placed superficially had ruptured a venous emissary at the junction of the sagittal sinus. A total débridement was performed with the patient receiving support throughout the operation. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the skull, laceration of the brain and acute subdural hematoma. Postoperatively, the extreme restlessness continued unabated until it was controlled by paraldehyde together with small dosages of morphine. Consciousness was regained on the third postoperative day and the remainder of the hospital course until his discharge on the twenty-first hospital day remained uneventful.

Repeated follow-up neurological examinations failed to reveal any abnormal findings. Subjectively, the patient complained of intermittent headaches and dizzy spells which became gradually less over the next year. He showed evidence of a change in personality and although he had been a heavy drinker always, this addiction became uncurbed. He developed pneumonia and died on January 11, 1941. This case illustrates the complication of an acute subdural hematoma associated with rupture of a large venous vessel. It emphasizes the necessity of immediate operative intervention. Also it suggests the unfortunate sequelae which develop from bilateral frontal lobe involvement. Figure 7 shows the size and location of the post-operative defect.

**CASE VI.** (E. N., age nine.) The patient was injured in a coasting accident on March 12,

1939. On admission the pulse was 140, the respirations 40, the blood pressure unobtainable and the color was poor. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the right frontoparietal skull, laceration and herniation of the brain with severe traumatic shock. There was a considerable loss of blood from the lacerated brain and the supportive therapy included two transfusions. The general condition improved and a total débridement was carried out three hours after admission. It was noted that approximately one-third of the right frontal lobe was destroyed. Figure 8 is a preoperative film which shows the location and extent of the fracture.

Follow-up records noted the presence of intermittent headaches, nervousness and irritability for the first four months after discharge. Repeated neurological examination failed to reveal any neurological abnormal signs. A shield was worn over the skull defect without any difficulty. Figure 9 shows some evidence of bone regeneration, but it has not been of sufficient degree to offset the need of a plastic repair.

This case illustrates the necessity of early intervention in those patients with marked non-localizing hemorrhage. Also it represents the type of case requiring further plastic repair when the size of the defect is too great to respond to natural bone regeneration.

**CASE VII.** (E. R., age thirteen.) On November 19, 1939, the patient was struck on the head by a heavy pulley which dropped thirty feet from the roof of an ice house. He was brought to a local hospital where he was found to be unconscious and in shock. Supportive treatment was given with a favorable response. When the general condition warranted moving he was transferred for operation, a distance of thirty miles.

On admission it was noted that he was stuporous but otherwise in relatively good condition. The blood pressure was 122/60, pulse was 92, and the respirations were regular. The peripheral reflexes were found to be depressed throughout. The right pupil was greater than the left but there were no other abnormal neurological signs elicited. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the left occipital vault, with laceration and herniation of the brain. The patient was brought to

surgery ten hours after admission and total débridement of the left occipital wound was performed. Intravenous support was administered throughout the procedure. Postoperatively, the patient's progress appeared to be satisfactory. He regained complete consciousness and the pupils became equal. The temperature remained elevated from 100° to 103°F. and finally on the fifth day he became increasingly irritable. This irritability was followed closely by several convulsions of the Jacksonian type which started with twitchings of the right face and then rapidly involved the entire body. Each succeeding convolution became more severe. Lumbar puncture was done showing an initial pressure of 400 with clear fluid. A diagnosis of subdural hematoma was made. A craniotomy was performed on the left side and approximately 100 cc. of encapsulated thick, xanthochromic fluid was removed. Postoperatively, the temperature dropped to a normal level within a short period. The hospital course from this point was uneventful and the patient was discharged on December 16, 1939. Figure 10 shows the size and location of the occipital postoperative defect, which is indicative of the severity of the injury. Figure 11 shows the site of the secondary operation for removal of a complicating subdural hematoma.

Follow-up records for the first year postoperatively indicated that the patient complained of headaches for the first three months. He was irritable and nervous. More recently he has been doing satisfactorily in school. Repeated neurological examinations have revealed a continued discrepancy in the size of the pupils, the left being larger than the right. The occipital cerebral lesion was above the calcarine fissure and there has been no residual visual field impairment. This case is an example of an associated subdural hematoma which did not become manifest until several days following the initial operation. Further surgical repair will be necessary to close the bony defect in spite of the absence of referable symptomatology.

CASE VIII. (F. K., age sixteen.) The patient was struck by an automobile October 30, 1940 and brought immediately to the hospital. On admission the diagnosis was cerebral concussion, compound comminuted depressed fracture of the right frontal bone and laceration and herniation of the brain. The blood pressure was 100/40, the pulse was 92 and the color was

poor. He was given supportive therapy and operated upon twelve hours after admission. Figure 12 is a film taken en route to the surgery showing the depth and extent of the depressed fragments. Figure 13 shows sketches of various steps of the operative procedure. The first one shows the location of the wound with the extruding cerebral tissue. The second sketch was made after removal of the herniating cerebral mass and reveals a small extradural clot and what appears to be a simple gutter-type depressed fracture. The third sketch illustrates the dural tears before débridement had been carried out. The postoperative course was uneventful excepting for a rise in temperature to a level of 102°F. over the period of the fifth to the ninth postoperative day. Chemotherapy which had been given for prophylactic purposes was discontinued resulting in an immediate response by the fall of the temperature to a normal level. Repeated neurological examinations failed to elicit any abnormal findings. The patient was finally discharged on the twenty-second hospital day free of complaints.

Follow-up records covered a period of ten months during which the patient has had no complaints. The most recent x-ray check-up (Fig. 14) shows evidence of bone regeneration.

This case is an example of the aid that may be derived from a single x-ray film when the inner skull table is more extensively fractured and depressed than was supposed. The pre-operative film (Fig. 12) evaluated more closely the severity of this lesion than was possible either by direct palpation or exposure. More value would have been derived, of course, had some of the fragments become widely separated and isolated. Also, this case is a good result from the point of view of minimal bone resection. Evidence of regeneration is present and any further repair will not be necessary.

CASE IX. (E. H., age twenty-four.) The patient was admitted on December 6, 1938 within a few minutes after sustaining the injury and was found to be in traumatic shock. Shortly after admission the patient had two severe generalized convulsions. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the skull involving both frontal bones with extension into the frontal sinuses and laceration and herniation of the brain. Blood and spinal fluid drained from the nostrils. The patient rallied

with support and was operated upon ten hours later. Both frontal lobes were found to be badly lacerated in the midline, and there was a hematoma present of moderate size. A total débridement of the brain and dura was carried out in the usual manner. There were two large fragments (Fig. 15) which were found to extend into the frontal sinuses and to involve both orbits. The blood supply to these fragments was considered to be adequate and they were therefore not totally resected. Accordingly, the bony edges were débrided and the fragments elevated. The dural defects were repaired with muscle grafts and the wound was closed without drainage. The patient made an uneventful recovery and was discharged on the twenty-fifth hospital day.

The follow-up records showed that she suffered from headaches and dizzy spells of an intermittent character for six months. Repeated neurological examinations failed to elicit any abnormal neurological signs. The patient, a nurse, returned to her work and has carried on continuously without any difficulty. This case illustrates the advisability of saving large fragments when the blood supply has not been affected markedly. Also, it emphasizes the advisability of the repair of all dural defects in the region of the paranasal sinus. Figure 16 demonstrates the condition of the operative site one year postoperatively. Marked regeneration of the bone is evident and no further repair is contemplated.

CASE X. (J. Q., age nine.) The patient was struck on the head on June 8, 1940, by a thrown baseball bat and brought immediately to the hospital. On admission he was found to have regained consciousness and his general condition was considered relatively good. He was given supportive treatment with prompt results. X-ray examination was performed (Fig. 17) and the patient was brought to surgery for operation shortly afterward. The diagnosis was cerebral concussion, compound comminuted depressed fracture of the right

frontal skull vault and laceration with herniation of the brain. A total débridement was performed. Postoperatively, the patient's hospital course was uneventful and he was discharged on the twenty-first hospital day. Figure 18 illustrates the size of the postoperative defect. This film was taken approximately six months postoperatively. There has been no evidence of any satisfactory attempt of bone regeneration during this period; consequently a plastic procedure will be necessary.

Follow-up records showed that the patient has suffered from headaches and some disturbance in equilibrium. A head shield has been worn with relief of the symptomatology associated with insecurity. The patient has done satisfactory work in school. There have been no residual abnormal findings noted in repeated neurological examinations.

#### SUMMARY AND CONCLUSION

A review of forty-two cases of major compound fractures of the skull vault associated with severe laceration of the brain has been presented. The study was based on 1,411 hospital admissions for craniocerebral injuries covering the period from 1937 to 1940. The rôle of the time element with respect to operative intervention and the factor of transportation have been reviewed. The principles of operative technic and the essential steps of the postoperative care have been outlined. Cases selected principally from the survival group for the purpose of emphasizing particular points in the discussion have been offered and the course of each summarized briefly. There have been no extensive changes advocated with respect to the neurosurgical technic, but a more conservative operative approach, as carried out in this series, has been suggested.



# A SYSTEM FOR THE MANAGEMENT OF ACUTE HEAD INJURIES\*

BASED UPON 1,000 PERSONAL CASES

MARK ALBERT GLASER, M.D.

Neurological Surgeon, Cedars of Lebanon Hospital

LOS ANGELES, CALIFORNIA

THOUGH operations upon the skull were performed in prehistoric times, the first recorded contribution to cranial surgery was that of Hippocrates (460-370 B.C.). Some of these early surgeons were extremely radical in their operative procedures, elevating all depressed fractures, separating linear fractures and drilling multiple holes in the lines of fractures. There operative mortality was extremely high being in the neighborhood of 90 per cent.

Dieffenbach,<sup>1</sup> in 1848, stated: "For many years I have feared more the operation of trephining than the outcome of cases of head injury which have come under my observations. Indeed, I have regarded the operation as a certain method of killing my patients." The handicaps resulting from poor operative technic, the belief that laudable pus was essential to the healing of wounds and an inadequate understanding of brain physiology were sufficient to discourage most of the surgeons who ventured into the field of brain surgery.

One by one these problems were solved. Lister introduced antisepsis in 1865. That the functions of the brain could be localized in the cerebral cortex was promulgated in a somewhat fantastic form by Gall (1757-1828), as organology or cranioscopy, and by his pupil, Spurzheim, as phrenology. Exploited by quacks and charlatans, phrenology soon became an object of derision among scientific men. Fritsch and Hitzig, in 1870, were the first to show that local body movements and convulsions could be produced by stimulation of definite areas

in the brain and that the removal of these areas would produce paralysis. Motor aphasia was localized by Bouillaud, in 1825, and verified by Broca in 1861. Focal epileptic spasm resulting from cerebral lesions were described by Bright (1836) and Jackson (1875) Ferrier (1876), Flechsig (1876) and Munk (1877) verified this work from an experimental standpoint, and also charted the sensory and motor areas; while Charcot and Pitres (1895) considered this problem from a clinical and pathological viewpoint.

The earlier brain surgeons, among whom were Macewen and Horsley, in England, E. von Bergmann, in Germany, and Fitzsimmons, Detmold, Keen and Abbe, in the United States, were still without the knowledge of the physiology and mechanism of increased intracranial pressure.

In 1901, Kocher,<sup>2</sup> and in 1902 Cushing<sup>3,4</sup> presented their experimental study on acute head injuries. Then for the first time a scientific basis was established for therapy in such cases. Surgery again held sway. The time honored subtemporal decompression was introduced. It seemed at that time that the entire problem of the treatment of head injuries was solved. The mortality was considerably reduced being in the neighborhood of 30 to 40 per cent. In 1905, Quincke<sup>5,6</sup> introduced lumbar puncture as a diagnostic and therapeutic measure. DeQuenu,<sup>7</sup> prior to 1912, and Jackson,<sup>8</sup> in 1922, utilized this method for the treatment of head injuries. In 1919, Weed and McKibben<sup>9</sup> paved the way for the clinical use of dehydrating agents. Soon

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these two methods, spinal puncture and dehydration, were merged and became the accepted method of therapy. This resulted in a further reduction of the mortality, which now ranged in the neighborhood of 7 to 16 per cent. During the period from 1919 to 1930, the value of spinal puncture was the subject of considerable debate, but there was a general tendency to favor its use.

Between 1930 and 1933, Coleman<sup>10</sup> and Dandy<sup>11</sup> began to realize the futility of this combination type of therapy in cases of hemorrhage, and being of the opinion that many hemorrhages were overlooked, advised a more radical use of multiple burr openings. Under the present existing surgical technic, these operations can be performed without mortality.

It is the purpose of this paper to point out that certain time established facts relative to the treatment of head injuries must be discarded and to suggest a simplified system of treatment. By classifying our head injuries according to variations of intracranial pressure, a more accurate diagnosis can be made and the regimen of treatment may be more scientifically carried out. By this means, it will be possible to readily differentiate the surgical from the nonsurgical case and more accurately outline the therapy for each group.

Even though we talk and write considerably about increased intracranial pressure in head injuries, the exact cause of this intracranial pressure is still a subject of debate (Shapiro and Jackson,<sup>12</sup> Rand and Courville,<sup>13</sup> Howe,<sup>14</sup> Weed,<sup>15,16</sup> Lehman and Parker,<sup>17</sup> Pilcher<sup>18</sup>).

The sole purpose of all diagnostic procedures in the care of acute head injuries is to determine whether or not an operable hemorrhage is present. Surgery is only indicated for hemorrhage and not for increased intracranial pressure due to brain damage. Increased intracranial pressure is not associated with all cases of head injury, and as a matter of fact, the majority of patients who die do so with a low

intracranial pressure. The experimental studies of Brown and Russell,<sup>19</sup> have demonstrated death from concussion without increased intracranial pressure. Consequently, to dehydrate indiscriminately every patient with a head injury who enters the hospital is without a scientific basis.

We have long assumed that the variations of pulse, blood pressure, respiration, pulse pressure and temperature are diagnostic of increased intracranial pressure. It has been our experience and the experience of others that such variations are not diagnostic of the rise of intracranial pressure and that the only accurate means of determining this rise is by spinal manometric readings. The variations of these clinical signs show the status of the patient, but they have no particular diagnostic value in determining the intracranial pressure. A massive intracranial hemorrhage of sufficient size to cause the death of a patient will always have an elevated intracranial pressure at some stage. It must be remembered that a patient may die from brain damage alone, and further, a small or large hemorrhage may occur with considerable damage. So it is quite evident that the removal of blood, even though it is a large clot, will not always save the life of the patient. It is only when the brain damage is of a nonfatal severity that the removal of hemorrhage will save the life of the patient.

Though the limitation of fluid intake has long been considered a means of reducing intracranial pressure, the work of Gurdjian, Webster and Sprong, as well as our own experience, has indicated that the limitation of fluid intake is not of particular value in the reduction of intracranial pressure.

With these fundamental points in mind, let us now follow a hypothetical case of head injury: Immediately after the injury the patient is usually in shock. The signs of shock are well known and consist of rapid, thready pulse, 120 pus; short, shallow breathing; cold, clammy extremities and skin; subnormal temperature;

diastolic blood pressure around 60; and pulse pressure around 50.

The treatment during shock includes absolute rest. All bleeding points should be controlled conservatively. Heat should be applied in the form of warm blankets, hot water bags to the great vessels of the extremities; shock cabinets, hot enemas of water or coffee. The foot of the bed should be elevated. Caffeine, pituitrin, strychnine, and atropine may be administered. Intravenous 10 per cent glucose should be utilized and transfusions are necessary if hemorrhage has been excessive. For restlessness the barbiturates, chloral hydrate, bromide and codeine are valuable. Attention should be directed to other injuries and particular note should be made of the cervical region, especially in regard to motility and pain. I have frequently found fractures of the cervical vertebrae masked by severe head injuries. Hemorrhage from the nose should be controlled by packs. Hemorrhage of the external auditory canal should be controlled by application of sterile dry cotton. Extensive neurologic examination should not be carried out. Surgery of all types, either head or body, is contraindicated at this time. Large lacerations of the scalp or compound depressed fractures are to be treated conservatively by the application of dressings or of hemostatic forceps to prevent hemorrhage. X-rays should not be taken. Morphine and dilaudid are to be avoided because they both are respiratory depressants; they change the size of the pupil and morphine raises the intracranial pressure.

After shock has subsided, a complete neurological examination should be performed. The variations of consciousness should be carefully observed, increasing paralysis noted, the pupillary changes observed and the reflexes repeatedly checked. It must be remembered, however, that the reflex changes are not always of diagnostic value. Further note should be made of the paralysis of cranial nerves, evidence of meningeal irritation and the presence of cerebrospinal leaks in the form of rhinor-

rhea or otorrhea. An otoscopic examination is advisable in order to determine whether there is a ruptured tympanic membrane or a blue bluging drum. From a clinical standpoint this is indicative of basal skull fracture, though it is not always verified upon pathological examination. Auscultation of the skull should be carried out to determine the presence of a bruit. This would be indicative of an arterial venous aneurysm. If there are open wounds of the scalp, the skull should be carefully palpated with a sterile gloved finger so as to determine the presence of any depressions. Occasionally, depressions are so situated that only tangential roentgen ray films will reveal their existence, and palpation quickly verifies the diagnosis.

During this postshock stage, primary suture of the scalp under local anesthesia should be performed if necessary. Tetanus antitoxin should be injected, hyperthermia combated with ice bags over the head, the great vessels of the neck and extremities, ice enemas given or the patient packed directly in ice for a period of five to ten minutes. If packed in ice, vigorous massage should be performed when the ice is removed in order to stimulate the circulation. In case there is a compound depressed fracture or a fracture through the sinuses, the sulfonamide compounds are indicated. The head of the bed should be elevated, chest secretions drained by posture, codeine and barbiturates given for restlessness; morphine should be used only if absolutely necessary. Coramine, caffeine, paredrine, adrenaline and ephedrine are valuable stimulants. The pulse, blood pressure and respirations should be charted every fifteen or thirty minutes, and rectal temperature recorded every one to four hours, depending upon the seriousness of the case. X-rays are not particularly important unless we are suspicious of hemorrhage. If so, good portable films may be obtained to determine the presence of depressed fractures, whether the fracture lines cross the middle meningeal artery and whether a pineal shift can be visualized. In our hands

electroencephalography has been a distinct diagnostic aid in determining the presence of extradural or subdural hemorrhage. Specific wave patterns have been described by Glaser and Sjaardema.<sup>20</sup>

In this postshock stage, we should avoid early elevation of depressed fracture, prolonged surgery of all types, protracted general anesthesia, irrigation of the external auditory canal, unnecessary moving of the patient, manipulation of fractures, airplane transportation and excessive dehydration. The signs of poor prognosis are increasing coma, rising temperature, irregular, rapid or Cheyne-Stokes respiration, increasing pulse, falling blood pressure, loss of sphincter control, dilated or pin-point pupils and absence of corneal reflexes.

If the patient is not responding well, as indicated by increasing coma or paralysis as well as marked variations in the pulse, blood pressure and a rising of temperature, a spinal puncture should immediately be performed, the pressure recorded and the presence of blood determined. If bloody fluid is removed, a blood count should be taken. In this way, the quantity of free blood can be compared with subsequent punctures. This gives an idea whether the hemorrhage is increasing or decreasing. Do not always remove spinal fluid at this time. Do not dehydrate at this time because by so doing the spinal pressure will be reduced and the original pressure will not be recorded. Having once established the basic spinal pressure, further manometric recordings are necessary to determine the progress of the patient. Based upon these variations in spinal pressure, the following classification of head injuries has been established. From this classification the proper therapy may be readily directed. Rodman and Neubauer<sup>21</sup> also considered surgery in those cases of high intracranial pressure as measured by the spinal manometer.

#### CLASSIFICATION OF ACUTE HEAD INJURIES BRAIN DAMAGE OR HEMORRHAGE

- I. *Spinal Block (unusual)*
  - i. Posterior fossa hemorrhage

- II. *Low Intracranial Pressure (60 mm. water or under)*
  - i. Traumatic
  - ii. Toxic dehydration
- III. *Normal Intracranial Pressure (60 to 200 mm. water)*
- IV. *Intermediary Intracranial Pressure (200 to 300 mm. water)*
  - i. Reducible intracranial pressure
  - ii. Increasing intracranial pressure
- V. *High Intracranial Pressure (300 to 700 mm. water)*
  - i. Reducible intracranial pressure
    - (a) Brain damage
  - ii. Persistent or increasing intracranial pressure
    - (a) Extradural hemorrhage
    - (b) Subdural hemorrhage
    - (c) Intracerebral hemorrhage

Classifications based upon gross or microscopic pathological findings are of extreme importance, but they give only the end results and are of no value in outlining therapy. It must be remembered that each patient has a combination of pathological lesions, such as contusions, lacerations, edema and hemorrhage. Basing the severity of the injury upon the period of unconsciousness and using this as a means of classification is also misleading and does not aid in suggesting the proper therapy (Glaser and Shafer<sup>22</sup>). To utilize the type and location of skull fracture as a means of classification is of little importance in the therapy, except when we are dealing with those of a depressed nature. It must be remembered that we treat brain damage and not skull fracture.

#### I. SPINAL BLOCK

In some instances a foraminal obstruction, either by partial herniation of the brain stem into the foramen magnum, or by pressure from hemorrhage in the posterior fossa upon the aqueduct of Sylvius, will give either a partial or complete block upon jugular compression. Occasionally, such a block may appear to exist due to artificial

obstructions in the needle, such as blood or bits of dura. Consequently, the needle should be manipulated, and the abdomen compressed to determine whether the fluid in the manometer will rise. If such an obstruction is actually present, cerebellar explorations, or the atlanto-occipital operations of Ody<sup>23</sup> may be performed. There are a number of successful cases in the literature reported by Briesen,<sup>24</sup> Tailhefer<sup>25</sup> and Zimmerman.<sup>26</sup>

## II. LOW INTRACRANIAL PRESSURE

**Traumatic.** Though we have seen only two such patients in this series, Leriche<sup>27,28</sup> reports twelve instances among seventy-five cases. He originally described this syndrome, finding a pressure of less than 10 with the patient seated; whereas, Stultz and Streicher,<sup>29</sup> in the prone position, found pressures in the neighborhood of 0 and 2. The clinical picture consists of well defined frontal headaches, associated with nausea, vomiting and giddiness, at times semicomma, but frequently torpor and mental stupor. Associated with this picture may be a positive Kernig test as well as slight stiffness of the neck. Though these cases are rarely of a serious nature, the symptoms can be relieved by injections of 20 to 40 cc. of distilled water intravenously or subcutaneously. If this is not followed immediately by improvement, the injections may be repeated, or 500 cc. of physiological sodium chloride may be introduced by the same methods. Leriche advises that the therapeutic results should be checked by further manometric readings.

**Toxic Dehydration.** This was present in this series, in several instances because of overenthusiastic osmotherapy and fluid limitation. An increase of fluid intake immediately cleared up the symptoms. These patients may become comatose and their temperature rise. Vomiting, sweating, acidosis and increased concentration of the blood with a very dry, thick tongue were prominent clinical symptoms.

## III. NORMAL INTRACRANIAL PRESSURE

The majority of patients with craniocerebral injuries do not have a high intracranial pressure. These patients get along quite satisfactorily with supportive therapy. Frequently, patients with a normal intracranial pressure have focal neurological signs due to localized brain contusion. These focal areas involved may also be determined by the electroencephalogram. Such patients usually recover rapidly because the brain damage is not extensive. Spinal drainage, osmotherapy or surgery are not indicated in this group. At times we encounter patients with or without focal signs, who have normal intracranial pressures and in addition have such severe brain damage that they die. A rupture of the Vein of Galen may also present such a picture (Bagley<sup>30</sup>). Acute cerebral hemorrhage may be present in patients whose intracranial pressure is normal. Such patients may die from severe associated brain damage, even before the hemorrhage has reached sufficient size to be of clinical importance. In these instances the intracranial pressure will be normal because the hemorrhage has not reached sufficient size to displace the brain. The intracranial pressure will also be low in acute cases of hemorrhage, if the readings are taken before the hemorrhage has become large or in patients who are in a state of extremis. In patients with a subdural hemorrhage wherein the bleeding is slow and does not reach any appreciable size until a period of several weeks has elapsed, the intracranial pressure may be normal or high, depending upon the ability of this hemorrhage to compress the brain locally. Normal intracranial pressure in head injuries has been described by Zierold,<sup>31</sup> Browder and Meyers,<sup>32,33</sup> Abramson and Mathews,<sup>34</sup> and Shapiro and Jackson.<sup>12</sup>

## IV. INTERMEDIATE INTRACRANIAL PRESSURE (200 MM.)

**Reducible Intracranial Pressure.** If an intracranial pressure is high, and we have

managed to reduce it by repeated lumbar taps, or osmotherapy, and if the reduction is maintained below the limit of 200, we may then assume that this is not a case of hemorrhage. Of course, these spinal pressure findings must always be taken in conjunction with the clinical picture. Should any doubt exist, surgery is indicated.

*Increasing Intracranial Pressure.* If the intracranial pressure is high and following spinal drainage the pressure is reduced, yet on repeated taps the pressure is found to have always returned to higher limits, the diagnosis of hemorrhage is likely. Such changes in spinal pressure, taken in conjunction with the clinical status of the patient, are indicative of hemorrhage and call for exploration. If in doubt, surgery is advisable.

#### V. HIGH INTRACRANIAL PRESSURE (300 TO 300 MM.)

*Reducible Intracranial Pressure: Brain Damage.* High intracranial pressure may be due to brain damage. This pressure may be reduced spontaneously, or be reduced by therapy. If spinal puncture drainage, or osmotherapy is carried out, and the pressure remains low and does not return to its former heights, and in addition, the patient improves clinically, hemorrhage may readily be ruled out.

*Persistent or Increasing Intracranial Pressure.* Brain damage alone will not always account for an intracranial pressure which returns to a high level after repeated reduction. This is suggestive of hemorrhage. When the other elements of the clinical picture are consistent with such a diagnosis, provided tumor or infection are ruled out, the neurological signs may localize the hemorrhage. Even if these neurological signs are of a multiple nature, hemorrhage should not be disregarded. A combination of multiple areas of brain damage, associated with separate hemorrhage, can give a number of localizing signs. Thus from a clinical standpoint we cannot always accurately localize the hemorrhage. In some instances a large hemorrhage will

be present and surgery will cure the patient, but in other instances this hemorrhage will be combined with fatal brain damage.

#### SURGERY

In cases of high intracranial pressure not associated with hemorrhage surgery is of no value. In such cases a subtemporal decompression may do more damage than good. These operative decompressions fail to reduce the pressure equally throughout the brain and leave a local congestion with swelling and edema, thereby defeating the purpose of the operation. The brain may bulge into the operative wound, cause additional trauma, and seal the opening caused by the decompression so tightly that if free fluid were present, it could not seep out even if a drain were inserted. The small opening itself will not permit sufficient volume of brain to protrude to cause a lowering of the intracranial pressure (Heuer,<sup>35</sup> Munro<sup>36</sup>). For these types of injury conservative reduction of pressure is indicated.

Mass displacing lesions, secondary to trauma, may be due to hemorrhage or to subdural collections of fluid. The hemorrhage may be located extradurally, subdurally, intracerebrally (Courville and Bloomquist<sup>37</sup>), or intraventricularly. In some rare instances hemorrhage may appear in the posterior fossa which necessitates exploration of this area.

If a diagnosis of hemorrhage is made and accurate localization is impossible, it is well to carry out multiple burr openings on one or both sides of the skull, so that the underlying brain may be inspected. If a hemorrhage is found on one side and the patient does not progress satisfactorily, the other side should be explored (Gurdjian,<sup>38</sup> Peet<sup>39</sup>). Frequently, we operate on both sides immediately. Should there be definite clinical signs of hemorrhage and none found either extradurally or subdurally, cerebral puncture should be carried out for suspected intracerebral bleeding. If a hemorrhage is found within the meninges, the

skull opening should be enlarged, the clot completely evacuated and the bleeding points coagulated or ligated. As brain damage is combined with most cases of hemorrhage, osmotherapy and spinal drainage should at this time be used in conjunction with surgery.

The treatment of depressed skull fractures is based upon the experimental work carried out by Naffziger and Glaser,<sup>40</sup> and the clinical studies of Glaser and Shafer.<sup>41</sup> Depressed fractures may be divided into simple fractures with rounded depressions, or with spiculated depressions, and compound fractures with rounded depressions or comminuted and spiculated depressions. The objective in the treatment of these fractures is two-fold: that of rendering emergency care for the associated brain damage or hemorrhage and that of restoring the cranial defect. If simple rounded fractures or simple compound fractures are present over nonfunctioning areas, elevation is not essential. If one is in doubt as to the character of this depression, elevation is indicated. Clinical and experimental evidence indicate that the underlying pathological condition in the brain is caused by the original blow and not by an irritation of a rounded depressed portion of bone. In cases of compound depressed fractures again emergency elevation is not essential. If the condition of the patient does not warrant operative intervention, these compound wounds may be converted into simple wounds by primary suture of the scalp. All surgery should be performed under local anesthesia. The bone may be held in place over an intact dura by simple placement of these fragments or by holding these fragments in place by a catgut screen. If large blocks of bone are to be removed, the use of the precision pneumatic saw, described by Glaser, can be utilized.

#### CONCLUSIONS

1. A classification based upon the variations of intracranial pressure has proved

more valuable for the treatment and proper interpretation of patients with head injuries than classifications based upon skull fracture or pathological considerations.

2. Acute hemorrhage of sufficient magnitude to prove fatal in cases wherein the brain damage is not a factor in the patient's death, will always give a high intracranial pressure at some stage prior to death. If the pressure is taken too early, that is before the hemorrhage has reached sufficient size to increase the intracranial pressure, it naturally will be low. If the pressure is taken when the patient is in extremis, the pressure may also be low. This does not apply to cases of subacute and chronic subdural hematomas because in such instances the hemorrhage arises slowly enough actually to compress the brain without increasing the brain volume within the intracranial cavity. The intracranial pressure in such instances may be either high or low.

3. If the intracranial pressure is high and following spinal drainage the pressure is reduced, yet on repeated taps the pressure is found to have always returned to higher limits, the diagnosis of hemorrhage is likely. Such changes in spinal pressure, taken in conjunction with the clinical status of the patient, are indicative of hemorrhage and call for exploration. If in doubt, surgery is advisable.

4. Lumbar puncture is without danger if the fluid is removed slowly and the original pressure only halved. It is invaluable for the proper evaluation and interpretation of the case of head injury as well as for the reduction of an increase in intracranial pressure.

5. The localization of hemorrhage by clinical signs alone is frequently impossible because the hemorrhage may be bilateral, or the hemorrhage may be combined with multiple brain damage. In such instances, the pineal shift, the electroencephalograph, pneumoencephalogram, or multiple burr openings are the methods available for diagnosis. In the acute cases, the pneumoencephalogram is contraindicated.

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# POSTOPERATIVE THROMBOSIS AND EMBOLISM\*

GORDON MURRAY, M.D.  
Surgeon, Toronto General Hospital

AND

Ross MACKENZIE, M.D.  
Demonstrator in Anatomy, University  
of Toronto

TORONTO, CANADA

*Infective Phlebitis.* The tendency of writers<sup>14,15</sup> in recent years is to consider thrombophlebitis an infective process.<sup>15</sup> In an attempt to learn something more about this disease a series of 877 cases have been studied. This number includes the post-mortem records of 306 cases, 355 clinical cases of this disease which were treated by orthodox methods and 218 cases treated by the use of heparin, sixty-three of these having had pulmonary embolism before treatment was started. In those cases in which the records were complete, 35 per cent had redness, swelling and tenderness localized to the course of the long or short saphenous or both these veins with pitting on pressure localized to this area. In three cases there was an infective focus such as an ulcer and in ten an obvious streptococcal cellulitis or an infective lesion of the foot or toes with lymphangitis or lymphadenitis. The temperature in these cases was of the septic variety, varying between 100° and 104°F., and the leukocytosis varied between 13,000 and 31,000. There was considerable pain and much tenderness over the course of the vessels involved. The remainder of the leg and foot showed little or no swelling and otherwise was normal in all respects.

In some of these cases either the long or short vein contained hard, indurated, easily palpable masses which are probably evidence of thrombi, but many had only diffuse inflammation limited to the region, and a hard cord palpable in the course of the vein. In the latter group with rest in bed, elevation and moist dressings with heat, the inflammation subsided rapidly and within twelve days most of the symptoms and signs had disappeared leaving no edema and no ill effects. This probably is

the picture of an infected periphlebitis. This disease may recur at intervals and each attack tends to run a more or less similar course. In another group with varicose veins, hard indurated isolated masses make their appearance. The infection in these cases may provide one of the many conditions necessary for thrombosis, which latter condition is an accidental occurrence and not an essential part of the disease.

*Suppurative Phlebitis.* In sixteen of these cases this process went on to suppuration requiring drainage of multiple abscesses situated within the lumen and surrounding the vein wall. The clinical course of these cases was one of general malaise from the toxemia of infection, with high fever, leucocytosis, furred-tongue, marked localized signs of infection with pain, swelling, redness, tenderness and fluctuation.

*Pyemia.* Occasionally, this suppurative process, especially under certain conditions and if neglected, extends throughout the clot in the lumen of the vein. When it reaches the periphery of the clot or when the latter is broken up by bacterial enzymes, masses of pus may be discharged as emboli and carried to distant sites producing a pyemia. This occurred in only five of our cases.

The source of the trouble in these cases is probably an infected area causing a cellulitis and lymphangitis. As the lymphatics follow the course of, and are closely related to the veins, the walls of the latter may become involved in the inflammatory process, and thrombosis occurs as an accidental process. When thrombosis does happen it is the result of these organic

\* From the Department of Surgery, University of Toronto, Canada.

structural changes in the wall, and for that reason the thrombus is firmly attached over a wide area, probably accounting for the infrequency of massive pulmonary embolism in this particular type of the disease. Pulmonary infarct which did occur in two cases, produced lung abscesses requiring drainage, and cultures from the abscesses grew identical organisms to those grown from the primary focus, i.e., streptococcus from pelvic abscesses, etc.

In the lateral sinus, where this complication is prone to occur, the phlebitis is again, secondary to an inflammatory process surrounding the vessel and extending to it from an adjacent suppurative process in the mastoid, middle ear or brain. Occasionally, a suppurative process in the abdomen, groin, chest, neck, axilla or deeply in muscles or cellular tissue will produce conditions resembling very closely, those of lateral sinus thrombosis and suppuration. Massive pulmonary embolism rarely occurs in this type of phlebitis according to the records.

*Non-infective Phlebitis.* The commoner type of phlebitis occurring in most of the cases in our group, presents quite a different clinical picture and course. The most outstanding feature is swelling and the many terms, white leg, milk leg, phlegmasia albadolens, etc., which have been used since the time of Celsus, indicate the chief characteristics of the disease. The onset of the disease is usually in a patient confined to bed with a fairly severe illness or post-operatively, or if going about there may be a tumor or a pregnant uterus. Almost all of the 877 cases in our group had some other disease and the phlebitis occurred as a complication. As will be seen from the list given, many of these had diseases which cause some impairment of circulation.

#### Chest

- Coronary disease
- Rheumatic heart disease
- Chronic degenerative myocarditis
- Subacute bacterial endocarditis
- Pericarditis
- Pneumonia
- Syphilis aortitis

Carcinoma of the lung
Empyema
Fractured ribs
Bronchiectasis
Pulmonary tuberculosis
Lung abscess
Heat stroke
Syphilitic aortitis
Cardiospasm
<b>Abdomen</b>
Acute appendicitis
Appendicular abscess
Pylephlebitis of portal vein
Carcinoma of stomach
Duodenal ulcer and peritonitis
Carcinoma of bladder
Enlarged prostate
Carcinoma of prostate
Gastritis
Sarcoma of lymph-nodes
Bowel obstruction
Carcinoma of pancreas
Jaundice (hemolytic)
Carcinoma of cecum
Ulcerative colitis
Jaundice with stone
Carcinoma seminal vesicle
Hemorrhoids
Ventral hernia
Carcinoma of colon
Inguinal hernia
Bladder stone
Strangulated inguinal hernia
Chronic Bright's disease
Diverticulitis
Carcinoma of rectum
Carcinoma of gallbladder
<b>Orthopedic</b>
Acute infective arthritis
Fracture spine
Fractured neck of femur
Ingrown toe nail (septicemia)
Fractured olecranon (open reduction)
Dislocation of femur
<b>Gynecological</b>
Endometriosis
Carcinoma of ovary
Cyst of ovary
Septic abortion
Cesarean section
Pregnancy
<b>Head</b>
Brain tumor
Carcinoma of tongue
Cerebral concussion
Brain abscess
Endothelioma of pharynx
Carcinoma of larynx
Carcinoma of mouth
Cerebral hemorrhage
Carcinoma of pharynx
Gangrene of legs
Cellulitis of foot
Chronic cellulitis with ulceration
Pernicious anemia

Osteomyelitis  
Secondary carcinoma  
Meningitis  
Diabetes  
Gonorrhœa  
Thrombophlebitis migrans  
Sarcoma of thigh  
Endothelioma  
Syphilis of spinal cord  
Disseminated sclerosis  
Burns

The first evidence of the disease in some patients may be a sudden occurrence of an infarct in lung, in 12 per cent or a fatal pulmonary embolism. In the others either swelling of one or both legs or aching pain in calf or thigh occurs. In many cases with severe infections such as pneumonia or peritonitis, etc., or after major operations, the reaction as shown by malaise, fever, leukocytosis, etc., overshadows the picture. In other non-infective cases such as normal pregnancy, chronic degenerative myocarditis, etc., there is very little general malaise, a temperature which averaged 100 degrees and only a slight leukocytosis. The onset in some may be a sudden acute pain frequently in the calf, popliteal space, adductor region of the thigh or over the femoral vessels in the groin. This with the color and temperature changes may be mistaken for embolism. The swelling, even if slight, the presence of some warmth, and pulsations at the ankle, even if difficult to feel at times, are distinguishable from embolism with its shrunken, cold, white periphery without pulsations. The swelling involves the foot, leg, thigh and sometimes the buttock and lower abdomen and occasionally reaches the axilla. It is diffuse and in the earlier stages pits on pressure. There may be no redness of the skin, (65 per cent) although there may be variations of color such as indistinct mottling, a faint pinkish color which is diffuse and not related to any definite area of venous channel, or more commonly very faint bluish white color, from which its name is derived. The nails may be cyanosed. Slight tenderness on pressure, of ordinary edema is present, but there is no marked tenderness except over areas in the course of the thrombosed

superficial or deep veins in the calf, thigh, inguinal region, or over the course of the external or common iliac veins. Occasionally, digital examination of the pelvis will reveal tenderness in the lateral wall on one or both sides which may be related to a similar process in the internal iliac veins and their branches. With continued pressure over the femoral veins to displace the edema fluid, a longitudinal cord can be palpated in many cases, which has been proved on operation to be<sup>1</sup> the thrombosed femoral vein. In none of our cases in this group did suppuration or pyemia occur.

Altogether this is not the picture of an acute infective process. More evidence to support this view was obtained when at operation to ligate thrombosed veins, segments were excised in ten cases and anaerobic and other cultures of the perivenous tissue, vein wall and contained clot, were made. No growth of organisms was obtained. This of course does not rule out the possibility of a virus infection. Pulmonary embolism occurred in 349 cases and in 32 per cent of these cases it was fatal within a few minutes while 68 per cent died of the effects of partial pulmonary obstruction after six hours to several days and at postmortem examination multiple infarcts were found. Cultures in these cases failed to show the presence of organisms except in two cases. In another case suppuration was thought by the pathologist to be present on examination in the gross, but cultures failed to grow organisms.

Of those cases which survived and showed definite clinical and x-ray evidence of infarcts, most did not develop lung abscesses, empyemas or other evidence of infection. In two cases lung abscesses did ensue. It might be inferred that the abscess resulted from secondary infection of the infarct and not from bacteria carried in the embolus because the organisms cultured from the abscess were a mixed flora, similar to postaspiration abscesses and not a single organism such as the streptococcus obtained from pelvic cultures in such cases as postpartum, infection, etc. Moreover, the

onset of the abscess was delayed and did not develop with a chill, high fever, etc.

In over 200 animal experiments<sup>11</sup> also, by aseptic technic, aseptic thrombi were produced in veins of the extremities. Cultures of the perivenous tissue, vein wall and contained thrombus, did not grow organisms. Section of this tissue, both in the gross and under the microscope, resembled very closely the sections of thrombosed veins removed at operations on patients and at postmortem examinations. Moreover, the fact that heparin in appropriate amount prevents such thrombosis, points to some other factor than infection, causing thrombosis.

The predilection of the disease for the left leg in 68 per cent of cases, even in cardiac or other remote lesions, or in right-sided abdominal operations such as for appendicitis or hernia, seems to favor the non-infective theory. Also the extensive aseptic portal thrombosis that occurs frequently after splenectomy favors this view.

Two hundred eighteen patients with acute thrombophlebitis in the Toronto General Hospital have been given heparin intravenously. As heparin has no special effect on infectious processes *per se*, the rapid clinical improvement must be attributed to its effect on thrombosis, which probably adds more evidence to the non-infective theory regarding the cause of thrombophlebitis.

#### PATHOLOGY

A photomicrograph (Fig. 1) of a section of radial vein of a dog removed four hours after an aseptic thrombus had been produced experimentally, shows a homogeneous mass of platelets and strands of fibrin including some red and white blood cells in areas, plugging the lumen. The intima is unchanged and the media, adventitia and perivenous tissue show no signs of inflammation. It has been demonstrated experimentally in animals that an occluding mass of this sort can be removed from a vein, or a similar mass which had been placed in an artery can be removed within

six hours, and no change in the vessel wall can be detected on microscopic examination and the vessels resume their function

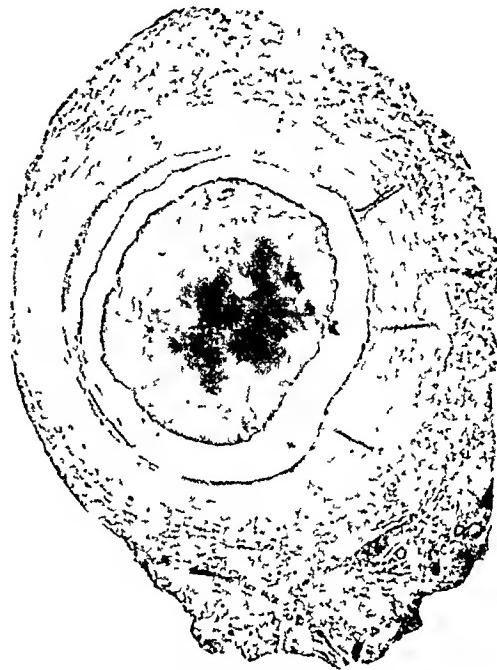


FIG. 1. Low power of section of radial vein of dog removed four hours after aseptic thrombosis.

indefinitely. Fig. 2 shows a vessel removed twenty-four hours after thrombosis occurred. There is no change in the intima in the gross and leukocytes are beginning invasion of the plug. If, however, the plug is left in the vessel, either vein or artery, for forty-eight hours, a great change has taken place. (Figs. 3 and 4.) The same mass occludes the lumen but polymorphonuclear leukocytes are invading it at the periphery. The intima is less clearly defined, the endothelial cells are swollen, and the outer coats of the vein wall as well as the perivenous tissue are also invaded by leukocytes. It has been shown experimentally that removal of the plug at this stage will be followed rapidly by a thrombus at this site. Clinically also, removal of a peripheral arterial embolus after forty-eight hours usually gives a similar result. In seventy-two hours Figure 5 shows the change in vessel wall, and Figure 6 at five days shows extensive invasion of the thrombus, vessel wall and perivenous tissue with granulation tissue and leukocytes so that in many areas

there is difficulty in distinguishing between the thrombus and the wall. At one area there seems to be an effort at recanalisa-

to have an influence in producing a thrombus and probably the most important of these is a slowing of the rate of blood flow.



FIG. 2. Low power of vein of dog removed twenty-four hours after thrombosis occurred.



FIG. 3. Low power of vein of dog removed forty-eight hours after thrombosis occurred.

tion. At seven days (Fig. 7), the wall and thrombus are scarcely distinguishable in the homogeneous mass of organized tissue.

The production of thrombus in a vein has been studied by Osler, Best and McLean, and many others, but the studies in experimental extracorporeal thrombosis by Shionoya<sup>7</sup> have shown the process in action. The normal blood elements can be observed circulating through the tube. In the absence of anticoagulants, small drifts of platelets settle out in the region of irregularities in the tube, and the masses so formed increase in size fairly rapidly. Presently a few white blood cells then red cells become entangled in the mass. Welsh and Aschoff have shown that the first step in the building of a thrombus is the adhesion of masses of platelets to the vessel wall. The progressive deposition of platelets goes on until the mass causes sufficient slowing of the blood stream, then strands of fibrin are formed and finally the lumen is completely obstructed. The blood column, peripheral to that point, rapidly clots forming a red portion of the clot, consisting of a mingled mass of red cells, white cells, platelets and fibrin.

#### FACTORS FAVORING THROMBOSIS

*Retardation of Blood Flow.* There are certain factors that are generally conceded

Blumgart and Weiss<sup>8</sup> have measured the rate of blood flow from arm to arm in normal individuals and during disease in others, and have shown that the rate is decreased to one-third and in some cases to one-fourth of normal in some diseases. According to their investigations, the diseases, one or more of which have been present in most of our cases of phlebitis and pulmonary embolism, are those in which the rate of blood flow has been greatly reduced.

Apart from the weakened heart action from cardiac disease or from toxins from infections or other sources, there are many other factors that tend to retard the return of venous blood from the legs and pelvis. When a patient with a weak heart action is put to bed, the massaging action of the muscles of the legs on a venous system, normally well supplied with valves, is lost. Or when such a patient has an inflammatory lesion of the abdominal wall or chest walls or cavities or an incision in the abdominal or chest walls, the normal respiratory excursion is diminished, thereby putting out of action the abdominal muscles and diaphragm whose pumping action take a great part in the return of blood to the right side of the heart especially from the lower extremities. The presence of pelvic, abdominal, intrathoracic tumors or

a pregnant uterus may further retard venous return by actual pressure on the venous system. Varicose veins with incom-

at a slower rate, platelets, when blood is brought to a stand still either *in vivo* or *vitro*. It is possible that a certain rate of

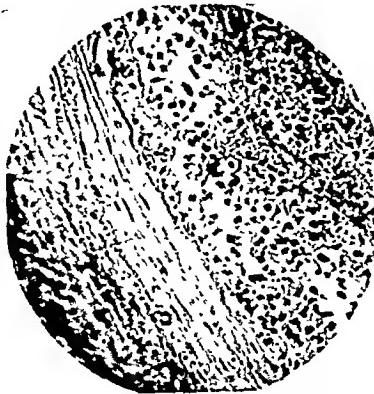


FIG. 4. High power of Figure 3.

petent valves provide areas where venous circulation is greatly retarded.

Under anesthesia and especially under spinal anesthesia, the heart rate is increased and its force weakened, the blood pressure frequently falls and during the operation the patient may be in cramped and unusual postures, there may be loss of blood and more or less shock, all of which make the circulation of blood slower throughout the peripheral vascular system. The patient is returned to bed and may be left lying for hours in a cramped position until the anesthetic and the depression from sedatives wear off. Tight dressings restrict respiratory movements and later pain and fright with dehydration from profuse sweating depress the circulation still further.

The changes produced by change of rate of blood flow are not known. The change in rate of flow in streams and rivers is responsible for the settling out of heavier particles near the shore while the lighter particles are carried beyond into deeper water as a result of which the delta is formed. It is conceivable that the fluid portion of blood with a definite specific gravity is able to keep the solid particles with varying differences of specific gravity, in suspension, solely because of the rate of flow. This must be true to a point at least, as can be demonstrated by the fairly rapid settling out of red blood cells, white blood cells and

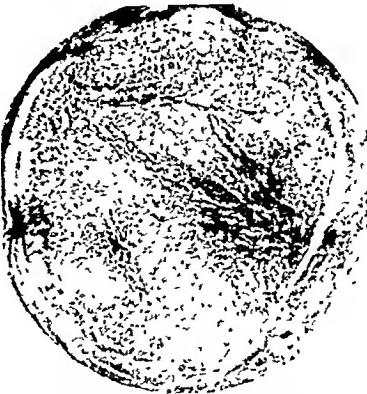


FIG. 5. Low power of vein of dog removed seventy-two hours after thrombosis occurred.

flow which is normal for the individual, is necessary to maintain the normal distribution of these heavier particles throughout the column of blood as it traverses the various segments of the vascular tree. We are familiar to a degree with the form and appearance of at least some of the formed elements in blood when they are at rest. Judging from the formation of some of these bodies, it may be possible that in the normal rapidly flowing blood stream their shape and contour may be changed. From the work of Ashoff it has been demonstrated that in the slowly flowing stream in capillaries and venules that the white blood cells are distributed mostly along the periphery and the red blood cells are in the axial stream. What the platelets are doing under these conditions is not known. The outline and form of a platelet at rest and in slow motion has been demonstrated, which is one of an irregular outline with multiple pseudopodia. In this form it is obvious that if placed at the periphery during slowing of the blood stream, they would grope along the intima and the pseudopodia would find anchorage in any defect, traumatic or otherwise, in the intima and would thereby administer first aid to any such lesion either individually or by grouping more and more of their numbers to produce desired effects. I am not certain,

however, that if in the rushing force and pressure of a rapidly flowing blood stream, the platelets may not assume a different



FIG. 6 Low power of vein of dog removed five days after thrombosis occurred

form and, as the gull in flight has feet stream-lined and invisible, but when retarding to alight the feet appear, so it is possible that the platelet may be in spherical form individually, or enclosed as a group as in the megalokaryocyte. Under the changing conditions of pressure and rate of flow, the pseudopodia may appear. While the change in rate of flow might be one force, physicochemical changes such as electrical attraction or repulsion between cellular elements and intima may also be a factor. Be these forces as they may, it has been demonstrated that heparin has two effects only: first, (Howell<sup>20</sup>), the prevention of clotting of blood and, secondly, (Murray<sup>21</sup>), the prevention of thrombosis. This latter effect would seem to indicate that heparin has some effect in preventing platelets either sticking together or sticking to roughened areas of intima. How this is accomplished is not known but it has been shown<sup>2</sup> that heparin is effective in this way either in a flowing stream or with the blood at rest.

*Physical Changes in the Blood.* There are many elements and properties of blood which are known to exist and which may play the more important rôles in thrombosis, but for which there are at present no methods of functional or quantitative measurement. Many of the salts and some other constituents have been investigated but no definite rôle in the formation of a thrombus or clot can be assigned to them with the exception of calcium. Prothrombin and fibrinogen variation have been measured by Bancroft and may help in predicting variations from normal in clotting times and thrombosis. It is not known what rôle other chemical or electrical changes may play in this process. Many investigators, however, have observed that the number of platelets in the blood stream bears some relation to clotting and thrombosis. The relationship between the diminished number of blood platelets and the prolonged bleeding and clotting times in hemophilia is well known. Less is known, however, of the effect produced by great increases in the number of platelets. One patient in our series in whom the spleen was removed for familial jaundice, had a platelet count of 250,000 before the operation. A continuous rise was followed for twelve days when the count reached 1,000,000. At this time the patient developed abdominal symptoms of pain, distention, vomiting, etc., and died in the next forty-eight hours of generalized portal thrombosis. Surgical literature contains reports of many such cases, but many other reports show platelet counts of over 1,000,000 and Shore and Kreidel<sup>9</sup> report one of 1,640,000 without evidence of ill effects. However, there is considerable evidence by Brock,<sup>10</sup> Krumbhaar,<sup>11</sup> Evans<sup>12</sup> and others that high platelet counts tend to coincide with shortened clotting times and a tendency to thrombosis.

*Damage to Intima.* It has been shown that sufficient damage to the intima of any vessel will cause thrombosis and occlusion of its lumen.<sup>2</sup> At every surgical operation many smaller and larger vessels are divided, and during parturition a multitude of

vessels are torn across and whether with ligature or without, they are closed with clots, thus setting in action a spreading process. Under normal conditions this is arrested at the next branch of the vessel where active circulation of blood is going on. Under abnormal conditions the spreading thrombosis may extend from pelvic or abdominal wall veins into the iliac or femoral veins, vena cava and practically all return channels and cause them to be occluded by the same process. While this might be an infective process there is some evidence as pointed out earlier, that in most of the cases it is not. It must be remembered, however, that a similar occlusion of femoral, iliac, saphenous or other veins may occur without damage to the intima of any of the vessels involved or their branches.

*Correlation of Symptoms and Finding to Pathological Changes.* The commonest symptoms of non-infective phlebitis are pain, tenderness along the course of vessels, swelling, temperature and the effects produced by pulmonary embolism. An attempt will be made to correlate these with the pathological changes found. As pulmonary embolism was the first evidence of disease in 17 per cent of cases, it can be assumed with certainty that in these thrombosis was going on quickly, extending into the lumen of the vessel involved and reaching such proportions that a mass large enough to produce pulmonary symptoms or death could break off and be carried through the venous channels to the pulmonary artery before there was any demonstrable change locally in the vessel wall to cause the thrombus to become adherent and to produce local symptoms and signs. (Fig. 1.) If the accident which caused the thrombus to become detatched or to break off, did not occur at that time, and the thrombus was allowed to remain quietly in its position in the vein for a longer period, probably three or four days, this would allow time for an inflammatory reaction to take place in the vein wall. (Fig. 6.) This reaction excited by the foreign body, the thrombus, fixes the

latter so that it cannot slip away, to cause the symptoms of pulmonary embolism. This may be an explanation of the fact so



FIG. 7. High power of vein of dog removed seven days after thrombosis occurred.

often stated, that pulmonary embolism occurs more rarely in cases showing clinical signs of phlebitis. It can be readily understood, however, that the first part of the thrombus to form might become fixed to the vessel wall in this way, but that the process of thrombosis and clotting might extend rapidly as a propagating thrombus, into new sections of the venous system, where the more recently formed masses may be broken off and swept away as emboli. This may be an explanation of the recurrent attacks of embolism within a few days. In 30 per cent of these there had been a pulmonary infarct or sentinel embolism and within a few hours or days another infarct or massive embolism caused sudden death. This reaction in the wall which has all the appearances of an acute inflammation with edema, polymorphonuclear infiltration, (Fig. 4) granulation tissue,<sup>12</sup> etc., would readily account for the pain and tenderness over the vessel involved. Before these signs of inflammation appear in the wall, there is no reason why there should be any elevation of temperature; but with their appearance a low grade fever would be expected and in 562 cases of the so-called non-infective group the average temperature was 99.8°F. This corresponds with the fever which occurs regularly from

protein absorption in all cases with moderate or large uninfected hematomas, e.g., extra dural hematomas, hemoperitoneum, hemothorax, simple fractures of larger bones, fracture neck of femur, etc. In the latter example, there is higher fever in intertrochanteric fracture in which there is a large hematoma than in the intracapsular type.

With the exciting cause of the inflammation—the thrombus—still present, the perivenous tissues become involved in the inflammatory process. As these tissues, especially in the common femoral and external iliac regions of the venous system, include practically all the lymphatic channels draining the leg, thigh and lower abdomen, as shown by Homans,<sup>13</sup> these channels readily become involved in the inflammatory process; and as they are confined mostly with the femoral sheath and are easily obstructed, which together with widespread venous obstruction, provide the common clinical finding of edema of the whole extremity. With organization of the thrombus vessel wall and perivenous tissue in one mass of scar, as has been demonstrated at operation by the author also by Neuhof<sup>1</sup> and others, the lymphatic channels are destroyed. Homans,<sup>13</sup> however, has shown that new lymphatic channels are formed in two to three weeks, which with the possible subsiding edema in the femoral sheath, in the cases with less severe inflammation, may account for the early clinical improvement in some cases. If, however, there is a more severe inflammation producing more scar tissue, there is greater permanent edema of the extremity. In such a leg with impaired venous and lymphatic circulation, recurrent attacks of cellulitis, ulceration, infection, etc., are common, and these further damage the lymph channels both at the site of infection and in the femoral and iliac regions, when the hard woody edematous leg results, resembling elephantiasis in many respects.

*Treatment of Non-infective Group.* If the foregoing evidence is true, it is obvious that some form of treatment to prevent throm-

bosis would be the ideal in this group. Some good general rules have been proposed to be followed in postoperative cases. These measures are practically all prophylactic and are directed toward improving the rate of return blood flow. They include: (1) correction of dehydration, of blood chemistry and treatment of shock; (2) shifting the patient about actively at short intervals, changing the posture in bed frequently and elevation of the foot of the bed; (3) deep breathing and leg and arm exercises as suggested by E. Pool and F. R. Braithwaite; (4) high caloric diet, high citrous fruit low protein diet as suggested by Bancroft and thyroid extract to produce temporary hyperthyroidism as suggested by Walters at the Mayo Clinic; (4) care in the use of tourniquets, avoiding any but the pneumatic type; (5) special care of varicose veins, by bandaging after operation, or by injection, attempting to cure them at least one month before operation and (6) gentleness and care at operation to prevent excessive tissue damage, to limit the amount of thrombokinase liberated. While all these improvements in nursing and surgical technic have diminished the proportion of postoperative embolisms, this dangerous complication is still very common. According to our postmortem records at the Toronto General Hospital, over 10 per cent of all deaths in this hospital<sup>14</sup> are due to this disease, and in 20 per cent of all postmortem examinations there are pulmonary emboli.

In an attempt to find some way to overcome this disease, experimental work on heparin was started at the University of Toronto in 1929 and is still in progress.<sup>2</sup> It has been shown that appropriate but harmless amounts of heparin given intravenously in dogs will prevent occlusion of veins and arteries following such injuries as produced occlusion by thrombosis in control experiments. Subsequently, heparin was given to patients in the wards of the hospital, and to date over 750 patients have received it intravenously. The patient experiences no sensations apart from those

of the ordinary intravenous injection and there are no toxic effects. Heparin *in vivo* will not dissolve a clot or thrombus and will not start a hemorrhage if the clotting time of the patient is kept below one-half hour. If, however, large or medium-sized vessels are not tied off at operation and there is any continued bleeding from these, or if conditions are such that a reactionary hemorrhage might occur, heparin will cause the bleeding to continue. For that reason the drug is not given for from one to four hours, or in some cases twenty-four hours following operation in which hemostasis has been doubtful. Sufficient heparin is given to keep the clotting time of the patient at about fifteen minutes, as determined by the Wright method. When the injection is discontinued the clotting time returns to normal in about one hour and the patient's blood is again in a state to occlude small bleeding vessels if a hematoma should be making its appearance. Hematomas have formed in four of the 260 postoperative patients, and in two of these it was thought that they would have occurred without heparin, but doubtless the heparin increased their size.

As it is thought that the thrombus which finally produces a pulmonary embolism or a large edematous leg, or both, begins, during the time when the patient's general condition is depressed by one or more of the many factors already described, the heparin injection is started as indicated after operation and is continued until the conditions thought to favor thrombosis have been corrected. When the patient has no pain, can breathe deeply with comfort, can turn over in bed and move about freely unaided, when gastrointestinal and urinary functions have been restored, and acute infections have begun to subside, the heparin injection is stopped. In some patients this may take three days but in others heparin has been continued for three weeks, the average taking about eight days. There has been no evidence of thrombosis or embolism in any of these cases.

It has been shown experimentally<sup>18</sup> that heparin will prevent thrombosis of the splenic vein after splenectomy combined with injury of the splenic veins. Clinically, heparin has been given to eleven cases of splenectomy in this hospital, in none of which did evidence of portal thrombosis appear.

In mesenteric thrombosis involving a limited segment of the intestinal tract, and requiring resection, the administration of heparin has been of great value in preventing extension of thrombosis postoperatively. The first four patients survived for two to four years. Two others died of infection but with no extension of thrombosis in mesenteric vessels.

Because of its action in preventing thrombosis, heparin was given as an experiment to 218 cases of thrombophlebitis of the non-infective type and sixty-one of these had already had multiple pulmonary infarcts. In all these there was a striking clinical improvement within twenty-four hours. The patient stated the pain in the leg was less or had disappeared and within seventy-two hours there was less edema, and what blueness or redness there was had disappeared. The patients who had had the pulmonary infarcts had no repetitions of these with the possible exception of three cases. The clinical course was much shortened and there was less edema remaining than in control cases. None of these patients died of pulmonary embolism.

While the processes in action to produce these effects are not known, it was thought probable that heparin stopped the progressive thrombosis that was going on and, therefore, the inflammatory reaction excited by repeated additions to the thrombus did not continue. The thrombus already established could not be affected so far as is known; and as the reaction to it was already established as shown by the clinical findings, it had an opportunity to heal. The injection of heparin has been continued about one week or more in these cases, or until symptoms are improved so

that the patient is able to be out of bed and to go about.

It has been shown that if a vein which has been injured severely enough to cause thrombosis in control experiments is kept patent by heparin for seventy-two hours, it will not become occluded; and on examination under the microscope the endothelium has closed over the areas of injury. This evidence has been used in support of this method of management of these cases.

The amount of heparin necessary to produce the required effect, namely, a clotting time of fifteen minutes, varies considerably in different individuals depending apparently upon variation in weight, muscularity and obesity. There appears also to be a considerable variation depending upon the condition or disease which has precipitated the attack of thrombophlebitis. Following certain of the more extensive operations in which we have found the clotting time to be diminished, there seems to be an increased amount of heparin necessary to obtain the desired clotting level. In other patients in whom as well as the phlebitis there has been massive pulmonary embolism, there also seems to be a greater amount of heparin necessary. Considering these factors, it is impossible to give a dose which is suitable in all subjects and for that reason the dosage must be adjusted according to the effect on the clotting time. In the average, however, it has required 1,000 to 1,800 units per hour of the heparin produced by the Connaught Laboratories of the University of Toronto. This is administered intravenously in normal saline, in a dilution which will give a patient a suitable amount of saline in a twenty-four hour period.

The length of time the administration of heparin should be continued is still under investigation. In the earlier stages we continued the injections for periods which now would appear to be unnecessarily long. However, as there are no positive criteria of the termination of the thrombosing processes or to indicate when the area is healed, our treatment has been stopped

purely on empirical grounds. The custom in an acute attack of thrombophlebitis, seen in the first two or three days of the disease, has been to discontinue the injections between the seventh and tenth days. If the case is seen later on in the second, third or fourth weeks, the inflammatory reactions are in an entirely different stage and as the reactions of continuing thrombosis cannot be predetermined, the response and the end results are less satisfactory.

If the administration of heparin after pulmonary embolism is considered, from our experience it seems to be an advantage to start this as early as possible after the embolism has occurred. Undoubtedly, if the attack could be predicted, heparin should be given before the thrombus has formed. It seems reasonable to assume that when any massive pulmonary embolism has occurred that a large part, if not all, of the unattached thrombus which remains free to break off in the blood stream has been detached, leaving the original site of thrombosis fairly clear of such masses. From most clinical histories there is evidence of repeated embolism at intervals of some hours to several days to support this view. If, however, heparin is started when there is very little remaining thrombus at the original site of the disease, there is the possibility that the formation of more thrombus will be prevented and further embolism may not occur. If, however, some days or hours have elapsed since the last embolism, it is more than probable that the original site in the venous tree has again become charged with newly formed thrombus. Even if heparin were started at this stage, it is not unreasonable to expect that some of these newly formed thrombi might become detached causing further embolisms.

It has been our practice, therefore, with this picture in mind to elevate the clotting time to the desired level of fifteen minutes and during the first three or four days to advise the patient to remain relaxed in bed hoping that any dangling thrombus of this nature may become attached to the walls

of the vessel and more firmly fixed so that it is less likely to break off. Hoping that this has occurred, after three or four days the patients are advised to begin exercising actively. Deep respiration, turning over in bed, voluntary energetic exercises of the lower as well as the upper extremities are encouraged; all of which encourage more rapid venous return and at the same time develop muscle, preparatory to the patient getting out of bed and resuming normal activities. After three days of such activity in bed, the patient is encouraged to sit up, get out of bed and continue active exercises while standing. The heparin injections are continued during these exercises. If there are no untoward effects such as a rise in temperature, increase of pain, swelling, etc., which happen only rarely, the heparin injection is stopped the following day. If it is at all possible, the patient is encouraged to exercise actively following this. Even if a patient must spend part of the time in bed, tranquility and repose are discouraged.

There are very many conditions under which thrombophlebitis makes its appearance, and in many of these it is impossible to carry out the routine described. Examples of conditions which make such treatment difficult are, spinal fusion, other orthopedic operations and during severe illnesses when it is necessary to keep the patient in bed for months. Under these conditions we have continued the injections for eight to fourteen days or until signs and symptoms have disappeared mostly, then the injection was stopped. However, even under these conditions, exercise of free extremities and deep breathing are vigorously encouraged.

Earlier in this series of cases, one was frequently disappointed to find that a swollen leg and symptoms were subsiding according to schedule, but, that swelling and symptoms appeared in the opposite leg during treatment. On first appearance this seemed to indicate that heparin was not preventing extension of thrombosis. However, on following many of these cases, I am convinced that the thrombus began in

the leg first affected; it extended through the iliac veins involving the bifurcation of vena cava with retrograde thrombi extending down the iliac and femoral systems on the opposite side, making this the dangerous source of emboli during this stage. The inflammatory re-action to the first formed thrombus, made its appearance on the first affected leg and with its latent period it followed the thrombus as it extended into the opposite leg, explaining the difference in time of appearance of swelling on the two sides. It is quite possible, therefore, that a thrombus might be present in the opposite leg when the heparin treatment was started but that the inflammatory re-action to the clot which is largely responsible for the clinical signs had not yet made its appearance. Under these circumstances, heparin injection has been continued until the second leg has gone through its period of swelling and then has returned to normal.

It has been our experience that there has been less residual edema when the patients have been treated with heparin early after the onset of symptoms. Enough time, however, has not yet elapsed to be certain of this or to know if there has been any influence on the incidence of varicose veins, ulcers, etc.

With persisting edema following thrombophlebitis either with or without heparin treatment, it may be important, during the earlier stages, to take precautions to prevent excessive edema at any time. The patient should be warned to be in the erect posture for only a short period at a time, lying down and elevating the extremities between times. There is some evidence to indicate that if a patient remains in the upright position too long, thereby allowing an enormous edema of the leg to appear, there is apt to be permanent injury and more persistent swelling than would otherwise occur. If, on the other hand, there is activity alternating with frequent periods of rest and elevation during the first few weeks, there may be a possibility of allowing development of collateral circulation in both venous and lymphatic systems which,

if not over taxed in the meantime, may ultimately be fairly adequate for return circulation in the future. During this period Buerger's exercises and pavaex therapy may be of some assistance, but I am not certain of this. If, in spite of adequate care, or if the occupation of the individual makes it necessary to be up for long periods and thereby some edema tends to appear, elastic supports, bandages, etc., should be worn to prevent overstretching of the venous and lymphatic pools distal to the main areas of obstruction.

Obviously, this routine of activity and exercise is not to be applied and obviously it is not safe to apply in cases of infective thrombophlebitis. In the other group, which has been called the non-infective group, there have been no evidences of ill effects or stirring up of inflammatory reactions by this regimen.

Several cases of acute infective phlebitis with cellulitis did not respond to heparin in the same manner as the non-infective group, which probably adds evidence to the theory that thrombosis in these cases, when it occurs, is a result and not a cause of the lesion.

Sulfonamide drugs should be given in the infective cases, but it does not change the course of the disease in the uninfected cases as would be expected.

The very wide spread investigation by Bancroft<sup>17</sup> has contributed considerably to the knowledge of thrombophlebitis. His work showed that by making special efforts in postoperative treatment the incidence of thrombosis and embolism could be reduced. The principle of speeding up venous return by various exercises, respiratory movements and frequent changes of posture in bed, massage, etc., during nursing care was of great importance. There is evidence also to support his method of postoperative treatment by sodium thiosulfate. This has been administered in doses of 10 cc. of 10 per cent solution on three successive days. It is uncertain what the specific effect of this drug may be. There is a possibility that the sulfur con-

tent may act similarly in some way to the high sulfuric acid content of heparin, either as an anticoagulant or by liberating heparin *in situ*. This aspect of the work requires further investigation.

With several forms of treatment available, any, or all of which may be more or less specific in preventing thrombosis and thereby eliminating embolism, it is obvious, that if, of the many postoperative patients, those who are likely to develop thrombosis could be selected, they could be treated and these complications eliminated. Probably the most important of the many interesting phases of Bancroft's<sup>17</sup> work is the attempt to discover those cases likely to fall into this group. By delicate estimations of prothrombin, he has been able to decide with fair accuracy those cases which appear to be safe from such complications, and to select those who are likely to run into difficulties from thrombosis.

Oschner's interesting contribution to the treatment of postoperative or other forms of acute thrombophlebitis is also of considerable importance. Novocaine block of lumbar sympathetic chains, in his hands has been of considerable value. His theory is, that the sympathetic nerve block relaxes arteries which are in reflex spasm as a result of the disease in the corresponding veins, thereby interrupting a vicious circle. In his hands most of the patients are greatly improved by the first injection. In some cases in which symptoms have recurred following this treatment, injection has been repeated on several occasions until a good result was finally obtained. There is considerable evidence from several other workers in this field that the results have been good. We have done an insufficient number to be able to be certain of the results. In the small number of patients on whom it was tried, we were convinced that pain in the extremity could be relieved almost immediately when a satisfactory block was obtained. When it was necessary to repeat the block because of return of pain, the symptoms were relieved on each occasion. We have not done a sufficient

number, however, to be familiar with the end results of this treatment.

Ramisection and resection of lumbar sympathetic trunk have been suggested but again we have not had sufficient experience on which to base an opinion.

Repeated intravenous injections of 500 cc. of hypertonic saline as advocated by Silbert for Buerger's disease have been tried. Unquestionably, in some patients there has been some relief of symptoms and recession of the inflammatory processes. In our experience, however, this treatment has not been of much value.

My experience with thrombectomy or attempts at ligation of vessels proximal to the area of thrombosis has not been sufficient from which to draw conclusions. From the many specimens studied at post-mortem examination, it would appear that the prospect of clearing successfully a thrombosed venous system with its many occluded tributaries, without at the same time dislodging some of the masses in the form of emboli, would be a matter of good luck. On the other hand, ligation proximal to the site of thrombosis, as advocated by Homans, is attractive and obviously would prevent embolism from the original site. However, there may be in this operation the possibility of forming another site from which thrombosis might extend. In my scant experience with this operation, there has been difficulty in localizing the proximal end of a thrombus which may be free and waving in the venous current. However, with efficient venography, the outline of such a thrombus may be shown and under these conditions the value of ligation proximal to the site can not be overestimated.

There are excellent probabilities that the work of Skofield, Lynd, etc., on dihydroxycoumarin may provide the best prospects for an anticoagulant to prevent or treat thrombosis. This substance has many advantages over heparin. Its prolonged action, administration by mouth, in an ambulatory patient, and its low cost are of the greatest possible advantages. If its

toxic properties can be eliminated and a suitable dosage worked out, there is every prospect that it may entirely replace the use of heparin. As there is a somewhat delayed action following its administration, it might be feasible to administer heparin or some other quickly acting anticoagulant when this was desirable, and to overlap and prolong the effect by dihydroxycoumarin by mouth. In operations on blood vessels in which it is desirable to have the effect immediately on the operating table, this plan might work out satisfactorily. Further work on the properties, toxicity and action of this substance is in progress and the results are awaited with great interest.

#### CONCLUSIONS

1. The possibility that most cases of phlebitis are not infective in origin is discussed.
2. The prevention of thrombosis by various forms of physical treatment and by drugs has met with some success.
3. The treatment of established thrombosis and its complications has been reviewed.

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VAGINAL hysterectomy clamp method provides most ample drainage, which is probably one of the factors that gives the operation its very low mortality.

# DIAGNOSIS OF ACUTE CONDITIONS WITHIN THE ABDOMEN IN THE PRESENCE OF DIABETES

JOHN D. WHITE, M.D.

Resident House Officer, Highland Hospital

ROCHESTER, NEW YORK

AND LEONARD K. STALKER, M.D.  
Surgical Staff, Highland Hospital

THE diagnosis of acute conditions within the abdomen, such as appendicitis, may be difficult when the patient has uncontrolled diabetes. This is due to the fact that many of the signs and symptoms of diabetic acidosis are the same as those resulting from lesions requiring surgery.

Unfortunately, the terms, diabetic acidosis and diabetic coma, are used interchangeably by some, and as a result only the terminal symptoms of hyperventilation and coma are associated with these conditions. However, the more common symptoms for which the surgeon is consulted are the abdominal symptoms, namely, nausea, vomiting, abdominal pain and tenderness which are usually associated with fever and leukocytosis.

These symptoms are present early in acidosis, as has been pointed out by Bothe and Beardwood in a review of a series of 1,260 cases of diabetes. In this group there were 136 cases of diabetic acidosis. Ninety-six, or 74 per cent of the 136 cases, showed as predominating symptoms either nausea, vomiting or abdominal pain. In those cases with abdominal symptoms, 85 per cent showed a leukocytosis of varying degrees, and 80 per cent had a fever.

Probstein and Drey reported a similar series of 1,343 cases of diabetes of which thirty-eight patients had frank acidosis. Twenty of the thirty-eight cases showed nausea, vomiting and abdominal pain, and in eighteen a leukocytosis was present. These authors also discussed the diagnostic problem as associated with nondiabetic acidosis, as in cases of cyclic vomiting or acetonemic crisis.

There has been no completely satisfactory explanation as to the cause of the abdominal symptoms presented by a patient in acidosis. Various mechanical, nervous and clinical possibilities have been suggested. Early writers have speculated that the condition was due to a dilatation of the stomach, hepatic engorgement or a diffuse pancreatitis. Autopsy and actual surgical reports now make it possible to say that none of these are important factors.

Wilder states that the explanation of pain in diabetic acidosis is to be speculative. It is his opinion that it is probably similar to the pain in heat exhaustion, as in both instances one is dealing with a marked loss of sodium, and in both the pain is rapidly relieved by the administration of sodium chloride or sodium bicarbonate.

Walker and others are in agreement with this mechanism, but believe that it is brought about by a chloride deficiency, and that first, due to an improper fat oxidation, acidosis develops, second, vomiting with a depletion of the body chlorides, and third, due to exercise and the chloride deficiency, the muscles become painful.

Popoff, Wills and Gray, and others have suggested that it is due to a state of anoxemia. The anoxemia is produced on one hand by a circulatory collapse with a resulting depletion of the actual oxygen carried to the tissues, or on the other hand, the tissues develop the inability to utilize the oxygen.

The association of an irritation of either the sympathetic or parasympathetic nervous system has been suggested, but careful neurological examinations have not confirmed this opinion.

It is obvious that the abdominal symptoms in acidosis are not due to the presence of a surgical lesion, because exploration, and in other instances, autopsy, has uniformly failed to find sufficient evidence against any abdominal organ to account for the clinical findings.

Only a small number of cases have been reported in which actual operation was done in the absence of demonstrable pathological conditions. Obviously, the cases reported do not represent the number of operations which have been needlessly done. McKittrick reviewed seven cases in which surgical procedures were performed during a phase of impending acidosis. In each instance the patient presented signs and symptoms demanding surgery, but in no instance was the abdominal disturbance at operation sufficient to explain these signs and symptoms.

De Takats states: "I have explored two normal abdominal cavities during diabetic coma and have delayed operation in a case of spreading peritonitis, due to perforated appendicitis; the latter died, the first two recovered." This has been the experience of many of us, and it seems to be an accepted opinion that if doubt exists and if the patient's general condition will permit, that a careful exploration would make certain with greater safety than would prolonged delay.

The onset of diabetic coma may be characterized by nausea, vomiting, obstipation, abdominal cramps, tenderness, rigidity, elevation of temperature, rapid pulse and a leukocytosis. On the other hand, the clinical picture of an acute abdominal lesion in a diabetic is frequently vague. The temperature, leukocytosis, pain and muscle spasm seem to be less than that seen in a nondiabetic. A marked acidosis and glycosuria are naturally present in the diabetic patient suffering from an acute condition within the abdomen.

The decision as to whether or not an acute condition within the abdomen is present should require frequent consultations of the surgeon and internist. As a rule

the diagnosis can best be made by instituting immediate treatment of the acidosis and observing the patient for a period of three to six hours. If the clinical picture has not improved, and in most cases the abdominal signs will completely disappear within this time, a surgical exploration should be seriously considered. Generally, if the abdominal signs are due to the acidosis, the pain, spasm and tenderness will be quite widely spread over the abdomen; and even though it seems to localize in the region of the appendix, there exists some degree of upper abdominal pain.

Abdominal pain preceding the onset of other symptoms speaks for a surgical emergency, particularly if the onset of pain is acute; while a gradual onset with polyuria and polydipsia preceding the abdominal pain probably means acidosis. It must be pointed out, however, that the onset of pain in acidosis may be acute, but the vomiting in these instances usually precedes the pain. If any doubt exists, an operation should be performed.

We have recently treated a patient in whom it seemed impossible to exclude the presence of an acute appendicitis in the presence of an impending diabetic acidosis.

#### CASE REPORT

Our patient, a man, aged fifty-one years, was admitted to the surgical service September 28, 1941. The referring doctor had made an admitting diagnosis of perforated peptic ulcer.

The patient complained of a severe mid-epigastric and right abdominal pain. He had been a known diabetic for five years and was taking some 60 to 80 units of regular insulin daily. Thirty-six hours before admission the patient became "sea-sick" while on a fishing trip. He was at first nauseated and then suddenly developed a severe epigastric and upper right abdominal pain. The pain was persistent, radiating through to the back. The patient was a somewhat irresponsible type of individual and apparently rarely examined his urine for sugar. He stated, however, that for the past few days he had had a poor appetite and that he was passing more urine than usual. The

day before admission he had decreased his insulin dosage, because he ate very little. Although he denied taking any amount of alcohol, we subsequently determined that he had consumed six or more bottles of beer while on his fishing trip.

The pain gradually localized to the entire right quadrant, but seemed more severe in the region of McBurney's point. Considerable nausea and vomiting of bile-tinged fluid accompanied this pain.

The family physician had been called and stated that the patient's entire abdomen was board-like and that a large dose of morphine was necessary to control the pain partially. At the time of admission, examination revealed an ill-appearing man who was approximately 68 inches tall and weighed 170 pounds. He was alert, co-operative and responded to questioning. His respirations were between 30 and 45 per minute, and the pulse was strong, averaging 110 beats per minute. The blood pressure was 135 mm. of mercury systolic and 80 mm. of mercury diastolic. Examination of the heart and lungs revealed nothing abnormal. The abdomen was diffusely spastic, but more definitely so throughout the right half. Definite midepigastric and upper right quadrant tenderness was present, but tenderness, grade 3 plus on the basis of 4, was localized to McBurney's point, and marked rebound tenderness was referred to this region. Rectal examination showed marked tenderness in the right iliac fossa. Temperature was 99.6° F. by rectum. The red blood count was 3,700,000 with a hemoglobin of 90 per cent (Sahli). The white blood count showed 24,000 leukocytes with 96 per cent polymorphonuclear cells. Urinalysis revealed sugar, 4 plus, and a trace of albumin. Roentgenographic examination of the lungs was reported as negative, and a flat plate of the abdomen revealed no evidence of intestinal obstruction, air under the diaphragm or renal stones. Blood was taken at this time but was not analyzed until the following day. It revealed a blood sugar of 455 mg. and a carbon dioxide of 22 volumes per cent, nonprotein nitrogen of 40 mg., and chlorides of 380 mg.

The patient was given 1,000 cc. of normal saline solution intravenously and 50 units of regular insulin. It was recognized that the patient was in a state of diabetic acidosis and consultation with the internist was held. It was the general opinion that in spite of the

obvious manifestations of the diabetic imbalance, that the patient had acute appendicitis and that immediate surgery seemed indicated.

Under spinal anesthesia, a right rectus incision was made. The appendix was in normal position, somewhat reddened and stippled, but did not appear abnormally diseased. The pathologist, however, was able to demonstrate slight polymorphonuclear cell infiltration of the wall of the appendix, but surgically speaking, no gross abnormal disturbance was demonstrated within the abdominal cavity. Appendectomy was performed, and the wound closed without drainage.

Immediately following surgery the patient was placed in an oxygen tent and given 250 cc. of blood plasma, both as prophylactic measures. Large amounts of intravenous glucose and saline were given together with insulin therapy throughout the next forty-eight hours. The patient at no time had more than one degree elevation of temperature, and made an uneventful convalescence. He was dismissed from the hospital on the sixteenth postoperative day.

#### COMMENT

This case illustrates the fact that it occasionally is difficult, in the presence of acidosis, to exclude a co-existent acute condition within the abdomen. It is progressively more difficult to be certain of the diagnosis when laboratory facilities are not easily available. Many of these cases are seen during the night when prompt laboratory service cannot be obtained and, therefore, the clinician must base his decision entirely on the evidence at hand.

Under ordinary circumstances we believe that the proper procedure is to treat the acidosis for three to four hours, and then reconsider the question of any underlying abdominal condition. If an acute condition within the abdomen is still suspected, surgical intervention should be based entirely on the degree of acidosis present.

Operations can be undertaken with a fair degree of safety with a blood sugar two to three times normal, provided that the carbon dioxide is not below 40 volumes per cent. In the case which we have presented

the presence of acidosis was apparent, but after fortifying the patient with some treatment for his diabetic acidosis, the abdominal symptoms did not subside as rapidly as we ordinarily expect. Inasmuch as considerable doubt remained in the minds of those treating the patient, operation was performed. Spinal anesthesia was considered the safest anesthesia that would accomplish the desired effect, and we doubt that any other anesthesia could have been used with equal safety.

Although these patients present an interesting and difficult diagnostic problem, the most interesting factor is the mechanism by which this abdominal picture is produced. As we have mentioned, the picture is seen in individuals who have acidosis from reasons other than diabetes, so it seems that it is entirely related to the acidosis itself and not the diabetes.

There is no entirely satisfactory explanation for the abdominal symptoms; and although the administration of large amounts of sodium chloride will alleviate the symptoms, there is no evidence to prove substantially that a depletion of sodium or sodium chloride is the actual mechanism by which this picture is produced. It is not unreasonable to expect that the entire picture is associated with a general anoxemia which, in combination with a chemical imbalance, produces some direct effect,

either on the muscular system or the nervous system.

#### SUMMARY

Abdominal signs and symptoms are frequently seen in individuals with diabetic acidosis. The differentiation between this picture and a co-existing, acute condition within the abdomen may at times be difficult and surgical intervention necessary. No satisfactory explanation exists for the abdominal symptoms in acidosis, but the association of anoxemia is thought to be important. A case in which a diabetic acidosis existed and at operation no intra-abdominal lesion was demonstrated, was reported.

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# THE EARLY DIAGNOSIS AND SURGICAL TREATMENT OF ACTINOMYCOSIS OF THE HEAD AND NECK\*

O. SAMUEL RANDALL, M.D.

WATERTOWN, SOUTH DAKOTA

THE study of the progress, clinical manifestations and pathological status of actinomycosis makes one realize that this disease must be diagnosed early and treated surgically in order to prevent severe disability and obtain a permanent cure. It is too often that we obtain patients in an advanced stage of this disorder who have been treated with potassium iodide and similar therapeutic measures and who could have been saved from such effects if suitable, but perhaps radical treatment had been instituted. In general it is believed that we must treat this infection in the same manner that we treat cancer, that is, by complete excision if at all possible.

The institution of such measures depends in a large part upon the early recognition of the causative organism, and thereby confirming a correct diagnosis. In man, the ray fungus, actinomycosis bovis, is usually considered the ordinary cause of the disease. Due to the fact that it is extremely difficult to culture the pathogenic form, this method of diagnosis is not practical.

## MEANS OF IDENTIFICATION

This infection comes to us so frequently in an uncontrolled stage because it has not been correctly diagnosed. For this reason identification of the causative organism is an important factor in this study. Because the clinical history and physical findings in most cases are not pathognomonic, one must depend almost entirely upon laboratory findings for a final diagnosis. The sulfur granules are quite visible to the naked eye. They are best obtained by straining the pus through

several layers of gauze. The granules are translucent, sulfur yellow or brown in color, and they are best removed as a wet preparation made with strong sodium hydroxide on a glass slide, crushed and stained with Gram's solution. The lobulated colony with Gram-positive mycelial filaments may be distinguished under the low power microscope. The most reliable method in the writer's experience consists of centrifuging a large quantity of pus and embedding the sediment in paraffin. Sections are cut and stained with hematoxylin and eosin, and with Gram's solution. Characteristic colonies as in Figure 7 are then sought. Tissue from an area of liquefaction will generally show the granules. If it is taken from a dense indurated area without suppuration, the organisms will probably not be found.

A very interesting clinical pathological characteristic of actinomycotic abscesses and nodules is that although they may be quite large, tender and fluctuant, upon aspiration or incision they are found to contain a very small amount of pus. This is important also from the diagnostic standpoint. The first physician who sees these lesions has the best opportunity to obtain the organism on aspiration. Although only a few cubic centimeters of pus are obtained, this most frequently contains the colonies; while all subsequent punctures yield a dry tap or produce no granules, because the pus containing the granules frequently drains out in a short time. In some instances, it is very difficult to obtain the organism in pus from a sinus of long standing. One, therefore, should save all the material obtained from the first aspiration and study it both by

\* Studies of material from the Surgical Departments, University of Minnesota and Kansas University.

smear and by the stained sections for the characteristic colonies.

#### SECONDARY INFECTIONS

In view of the fact that these lesions are frequently secondarily infected by various bacteria, some authors such as Klinger, Colebrook, and Bayne-Jones have laid considerable stress on these invaders. Henrici on the other hand does not believe that they play an essential part in the pathogenesis of the disease since in metastatic lesions the ray fungus may be found without any associated bacteria, either in smear or on culture.

If death occurs acutely, it may be due to secondary infection (Hiss and Zinsser). Frazier stated that the suppuration was due to a secondary infection since actinomycosis was not a pyogenic organism. Graham, however, states that actinomycosis is a pus producer. Karsner believes that fever is usually due to this added infection which may result in a bacterial septicemia or pyemia.

#### GENERAL PATHOLOGY

It is upon a thorough understanding of the underlying pathological characteristics that proper surgical management rests. The principal features of the disorder of actinomycosis are as follows: (1) A granuloma is produced by an acute and chronic infectious process that progresses at the same time around the ray fungus. (2) The granulation tissue is composed of polymorphonuclear and mononuclear cells surrounded by a vascular zone: (Fig. 2) of epithelial cells, multinucleated giant cells, (Fig. 6) eosinophiles, and plasma cells. (Fig. 1.) This zone is in turn bounded by dense fibrous connective tissue. The vascularity of this granulation tissue is of great importance from the standpoint of operative treatment. (3) Along with the dense fibrous tissue reaction, there is a simultaneous degenerative process due to the invasion of connective tissue by the fungus. The former has a tendency to wall off and

to heal the infection, and the latter to advance the process by suppuration, degeneration and liquefaction. (4) When softening takes place, there is an extensive lipoid degeneration (Fig. 3) with production of abscesses, cavities and intercommunicating pus channels filled with purulent material containing yellow granules (sulfur granules). (5) Sinuses form and discharge purulent exudate. (6) The healing process is characterized by the formation of large nodules of cellular fibrous tissue. (7) Extension probably takes place by the mycelial filaments breaking off and being carried into adjacent tissue by wandering macrophages. (Figs. 4 and 5.)

#### SPECIAL PATHOLOGY

Different tissues respond in a fairly definite manner to actinomycotic organisms. The mucous surfaces of the body are rather resistant to the ray fungus. It is uncommon to find actinomycotic granulomas in mucous membrane; the organism tends to burrow away from such surfaces, and very often no trace can be found of the portal of entry in the mucosa. It is probable that the secretions in the oral cavity as well as in the gastrointestinal tract tend to prevent the growth of the organism. Also other primary lesions than those of the mucosa tend to heal (Wright, Kollie, Hetsch, Kaufman). Frequently, whether the case is of long or short duration, the portal of entry cannot be determined. The lesion may heal by cicatrization and by the dying out and absorption of the microorganism. As pointed out by Wright, complete healing may take place by destruction of the fungus in a lesion or possibly by their extrusion through a sinus.

Although it appears that some tissues are more resistant than others, any tissue may be invaded and destroyed by this infectious process. In man bone seems to be fairly resistant, but a periostitis is seen not infrequently. It is held by most authors that the lymph system is not involved, however, rare exceptions to this rule have been reported (Shiota, Werthamann). The

regional nodes are frequently hyperplastic, but it is certainly rare for extension to take place through them, or through the lymphatics. Although the infection is said to follow fascial planes, there are so many exceptions to this statement that it is of very little importance. Most of the growth takes place in the connective tissue, e.g., submucous, subperitoneal and subpleural tissues. Cope and Good state that there is a distinct continuity of the blood vessels in actinomycotic lesions. There are exceptions to this rule also. In fact, there is frequently rather marked fibrosis in the vicinity of the larger vessels of an organ and not infrequently one finds a direct invasion into the largest vessels, e.g., hepatic or portal vein, inferior vena cava, and lienal veins and small thrombi are noted in the smaller vessels. Although generalized infections do occur (Werthmann, Richter, Kissling), they are relatively uncommon by the direct invasion of the blood stream or by rupture of an abscess into a vessel. This is illustrated very well in Kasper's and Pinner's case of actinomycotic emboli to the heart with abscess formation as a metastasis from a primary focus in the arm.

In general, it may be said that the mouth is the most frequent portal of entry and localization of actinomycosis, while other portals of importance may be found in the lungs and intestines, and rarely in external lesions. From these foci, actinomycosis may actively invade every organ of the body by continuity or by metastases through the blood stream.

#### ACTINOMYCOSIS OF THE HEAD AND NECK (CERVICOFACIAL FORM)

This is the region of the body most often affected; most authors state that 60 per cent of the cases fall in this group. The upper jaw is rarely invaded, but the infection involves the gums, cheeks, teeth sockets, or the back of the mouth in the region of the molar teeth. The spread of the infection is away from the primary site toward the skin along the line of least

resistance. Later localization takes place as a small indurated area at the angle of the jaw, or as a more extensive condition



FIG. 1. A young colony and early granulation tissue reaction showing the characteristic zones.

involving the cheek in the parotid region. The parotid-masseter actinomycosis is the most typical and common form. There may be extensive invasion of the tissues around the mandible, but rarely is this bone involved by anything more than a periostitis, unless the infection starts about the socket of a diseased tooth. Submaxillary infection may occur as an infection along Wharton's duct (?), but the most common route is through the mucous membrane of the floor of the mouth. Low neck lesions may be due to direct extensions from the pharynx or trachea (?). There is generally little swelling on the inside of the cheek. As the lesions approach the skin during the course of softening and suppuration, numerous abscesses may occur in the involved tissues, and subsequently rupture through the skin to establish one or several draining points. The stage of induration may last several months. After drainage is established the condition may subside and very little extension may take place for a long time. Subsequently, there is more softening, abscess and sinus formation. Frequently, after a sinus tract has drained for a long time it closes by cicatrization. According

to Shiota, the acute features of this process depend, at least to some extent, on mixed infections.

progresses in the neck it tends to extend downward and sometimes backward. The muscles become infiltrated down to the

FIG. 2.

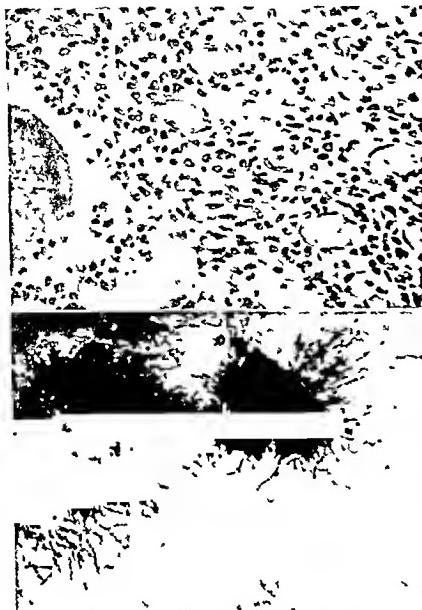


FIG. 4.



FIG. 2. The vascularity of actinomycotic granulation tissue.

FIG. 3. Lipoid degeneration in zone of increased vascularity.

FIG. 4. Colony made up of Gram-positive mycelial filaments.

FIG. 5. Actinomycosis of spleen; detached mycelial filaments surrounded by wandering cells.

FIG. 3.

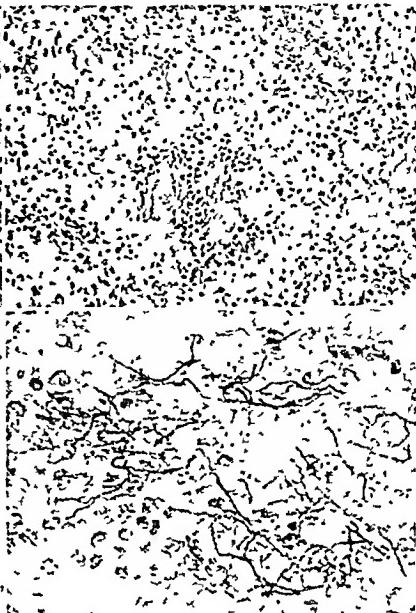


FIG. 5.



FIG. 6. Actinomycotic granulation tissue with numerous multinucleated giant cells.

FIG. 7. Microscopic paraffin section of centrifuged pus and stained with hematoxylin and eosin.

When lesions are seen early, there is apt to be considerable induration with very little localization and the borders of the process are ill defined. This is particularly true in lesions which become extensive in the cheek before obvious softening takes place. But in some cases suppuration and localization may occur early. From the parotid region, the process may extend into the temporal muscle, scalp, forehead or the back of the ear. As the lesion

base of the neck; direct extension into the mediastinum or the apex of the lung may follow. When the extension is backward, the vertebral column or base of the skull becomes involved, and subsequently the meninges and spinal cord are attacked (Moersch).

When the submaxillary region is involved, the extension is into the submaxillary gland, tongue, ribbon muscles of the neck and into the submental region.

The trachea is infrequently affected, even by secondary infiltration. The larynx may be primarily involved or secondarily eroded by actinomycosis of the head and neck, but the latter is unusual.

The patients first complain of a stiffness of the jaws and later of an inability to open and close the mouth completely. Then swelling occurs which may or may not be painful. Frequently, a dentist is consulted for toothache and in some of our cases teeth have been extracted. In some instances these patients on whom extractions were done had considerable oral sepsis and dental caries, so that dental hygiene and extractions were probably helpful. They may complain early of a facial pain which has been mistaken for trigeminal neuralgia. As was pointed out, the induration may persist for some time before suppuration takes place. The most common erroneous diagnoses are tuberculosis, malignancy and dental root abscess, or cervical abscesses, secondary to infected teeth. After these lesions exist for a while, there may be considerable cachexia and anemia with a low grade or hectic type of fever. When the condition becomes chronic, there is but little pain except when abscesses appear that need drainage.

#### THE TONGUE

Primary actinomycosis of the tongue is relatively rare and is usually secondary to actinomycosis elsewhere. The tongue is frequently the portal of entry, but by the time symptoms appear this primary focus has usually healed. In 1926, Figi brought the total of reported cases of primary actinomycosis of the tongue to thirty-nine. Cameron has recently presented two more cases, and in discussion of Cameron's paper, Shelmire quite appropriately pointed out that the rare lingual localization of the disease in man was more apparent than real. Cases have also been reported by Grupen, Barlow, Banister, Wanamaker, Mitchell and Venetianer.

Actinomycosis of the tongue in cattle is common, and in many of these bovine

cases particles of grain and straw have been found in the lesions. Fischer, Jurinka, Von Baracz, Schartan, Harm, Kockel, New and



FIG. 8. Case 1. Actinomycosis of neck in girl of thirteen.

Figi have demonstrated similar particles around actinomycotic lesions in the tongue of man.

It is most frequently seen in the anterior third of the tongue (rarely on the back of the tongue—Shiota), on one side along the margin and on the dorsum.

There is some induration of the tongue at the onset and the patient may complain of slight pain, stiffness and swelling. As softening takes place, and the lesion increases in size there is more disability. If the lesion is not incised, an abscess forms which may rupture and discharge purulent material. Multiple sinuses appear as extension takes place. Very rarely does a diffuse actinomycotic abscess of the tongue occur (Magnussen, Von Baracz), but a diffuse multilocular abscess with multiple draining sinuses may form (Cameron). From the tongue direct extension to adjacent tissues readily takes place.

There are two clinical forms of actinomycosis of the tongue: The first runs an acute course, with early suppuration simulating an acute pyogenic abscess. The other

form is more chronic, with more induration and occasional ulceration. This form may be mistaken for carcinoma.

mycosis in the United States only forty-two were in children. Figi reports that less than 3 per cent of approximately 450



FIG. 9. Case III. Girl age eight years, actinomycosis of right submaxillary region



FIG. 10. Case III. Lesion healed after wide dissection and euretttement one year later.



FIG. 11. Case VIII. Rapid extension of process with inadequate treatment.

#### THE DISEASE IN CHILDREN

In general, the clinical course and pathological findings in children are essentially the same as in adults. One gains the impression from literature that the disease is rare in children, but this is certainly not substantiated by the cases which form the basis of this report. In this relatively small series there were three patients under fifteen years of age. In 1925, Sanford and Vaelker found that in 670 cases of actino-

patients with the disease in his series were in children.

Children can be treated effectively if the proper methods are introduced and if the patients present themselves early enough. The treatment in children is the same as in adults, that is, surgery if possible. Likewise the prognosis is the same in children as in adults and that is favorable, if an early case is so located that it is accessible to surgery.

## PROGNOSIS

The lesions in the head and neck are much more favorable than actinomycosis

physically, and the lesions did not seem to progress very much for a time, this manifestation was only temporary; the



FIG. 12. Case ix. Actinomycosis of head and neck of two years' duration.



FIG. 13. Case ix. One year after radical excision of the actinomycotic process; no recurrence.

elsewhere in the body due to their accessibility and the likelihood of early recognition. There seems to be very little reason why all these cases should not yield readily to treatment and be cured if treated early enough.

## TREATMENT

Of the various forms of treatment, surgery, radiation and potassium iodide have proved to be the most valuable. Hyerdahl has reported good results with radiation therapy in actinomycosis of the head and neck, and prefers it in all types of actinomycosis to the exclusion of all other therapy. Magnusson has shown that actinomycosis in cattle is usually due to the actinobacillus and that massive doses of potassium iodide have been effectual but have had very little effect on lesions caused by the actinomycoses bovis. Reynolds and Henrici have shown that iodides have no effect on actinomycoses bovis *in vivo* or *vitro*. They obtained growth in media containing as much as 10 per cent potassium iodide. It was noted in several of our cases that although the patients felt better

patients died from the disease. Therefore, it is doubtful that iodides exert any specific



FIG. 14. Case x. Actinomycosis of the parotid-masseter region; two months' duration.

action on this parasite; and it is a question whether they stimulate fibrous tissue or not. It has not been possible to find any

reported cases of complete cure of proved actinomycosis by the use of potassium iodide alone, or of radiation therapy alone,

at first to do a complete extirpation of the disease process, as in cancer, since, in many instances promotion of adequate drainage



FIG. 15. Case XIII. Extensive actinomycosis right parotid and submaxillary regions.



FIG. 16. Case XIII. After six curettements lesion controlled one year later.

although some apparent remissions have occurred.

In attempting to treat the disease process, one must not rely on conservative

alone may cure the disease. However, one must follow these cases quite closely, and if the disease does not clear up, more radical methods must be employed.

One should not, however, limit his treatment to one form of therapy, but should use every accepted approach to cure that is known. It seems advisable to follow surgery with potassium iodide and adequate doses of deep x-ray in some cases.

Recently there have been reports on the use of sulfanilamide in these cases, but the follow-up time has been too short to make any definite conclusions as to its efficacy. In infections of the head, neck and tongue, surgery is preferred, viz., excision, if incision, curettage and drainage do not suffice.

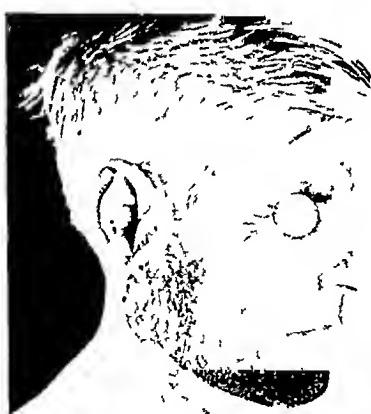


FIG. 17. Case XIV. Actinomycosis right parotid region extending into auditory canal and tonsillar fossa.

methods, for as a whole they have proved to be failures. Surgical measures such as incision, excision, curettage and drainage should have precedence over all other forms of therapy. It may not be necessary

#### COMMENT

The same principles of early recognition and adequate surgical procedures apply to actinomycosis of the thorax and abdomen. Brickner has reported success in abdominal cases using extensive surgical methods. But the abdominal and thoracic cases that we have encountered have not been treated with such success. It is believed that if these cases are diagnosed early enough and radical surgical excision employed, removing all dead tissue and

## COLLECTED CASES OF ACTINOMYCOSIS OF THE HEAD AND NECK—1925 TO 1940

Case	Hosp. No.	Sex	Age	Duration before Admission	Description of Lesion on Admission	Methods of Diagnosis	Treatment	Results
1	M.G.H. 608171	M (Fig. 8)	13	3 mos.	Moderately advanced right side neck	Paraffin section	Incision and drain; curettment (1 operation)	Cured. No recurrence 8 yrs.
2	M.G.H. A. B.	M	7	6 wks.	Right lower jaw and parotid region; sinus	Granules	Sinus tract curetted 2 operations	No recurrence 7 yrs.
3	M.G.H. B. A.	F (Figs. 9 and 10)	8	1 mo.	Hard mass 8 cm. submaxillary region right neck; no fluctuation	Smear	Wide dissection; curettment; one operation	No recurrence 4 years.
4	E.H. 35999	M	44	5 wks.	Early, right neck; no sinuses	Clinical sulfur gran. paraffin sec.	Complete endotherm excision; KI postoperative	Cured. No recurrence 8 yrs.
5	M.G.H. 60926	F	29	1 mo.	Moderately advanced left submaxillary and submental regions neck	Paraffin section	Excision and drain; two operations, KI	Cured. No recurrence 9 yrs.
6	M.G.H. 38703	M	65	5 mos.	Extensive mass right face and neck; many sinuses	Smear	Large doses KI incision and drainage; two courses deep x-ray	Cured. No recurrence 6 yrs.
7	M.G.H. 55891	M	40	6 wks.	Early lesions of cheek	Smear	Endotherm excision	Cured. No recurrence 10 yrs.
8	M.G.H. 33878	M (Fig. 11)	43	10 wks.	Extensive mass left face and neck; intra-oral ulceration	Smear	Incision and drainage; KI radium two courses x-ray	Death
9	M.G.H. 62058	M (Figs. 12 and 13)	46	2 yrs.	Localized to right head and neck	Paraffin section	Excision, drainage, curettment; two operations	Cured. No recurrence 8 yrs.
10	M.G.H. 57504	F (Fig. 14)	29	15 mos.	Fairly early left head and neck	Smear	Incision and drainage; KI; deep x-ray	Cured. No recurrence 5 yrs.
11	M.G.H. N. W.	F	35	3 mos.	Right cheek and angle mandible; indurated and fluctuant sinuses	Smear	Incision and cur-rettment dissec-tion submental glands	Cured 7 yrs.
12	M.G.H. L. E.	M	24	6 wks.	Mass 5 by 4 cm. left neck hard, not tender	Smear	KI (elsewhere) 1. Excision of abscess; 2, sinusex curetted 3, sinuses curetted	Followed 1 yr.
13	M.G.H. E. E.	M (Figs. 15 and 16)	55	10 wks.	Extensive mass right face and neck; sinuses, softening	Paraffin section	KI and x-ray (elsewhere). Currettement six operations	Control 1 yr.
14	M.G.H. J. F.	M (Fig. 17)	52	3 wks.	Mass right face and tonsillar fossa; sinus into auditory canal	Smear	Incision and cur-rettment; two op-erations	Incomplete fol-low-up
15	M.G.H. 61438	M	39	4 days	Anterior third mid-line tongue	Smear	Incision, drainage curettment; one operation	Cured 8 yrs.
16	M.G.H. 54637	M	43	13 days	Tongue and submen-tal region	Smear	Incision and drain-age; two opera-tions, KI deep x-ray	Cured 10 yrs.

exposing all actinomycotic channels, our percentage of success would increase. It is also believed that the reason most of the cases come to us so late is because an accurate diagnosis has not been made.

#### CASE REPORTS

This surgical approach can be facilitated with greater ease and obtain more certain and quicker results if an early diagnosis is made. This may be done by at least considering actinomycosis as the possibility in any infection of the head and neck of two weeks' or longer duration. This study is based upon the case reports given in tabulated form.

These sixteen cases have presented themselves to us during the last fifteen years. There was one death in this series. He was forty-three years old, with an extensive lesion on the neck of eleven weeks' duration and his treatment consisted mainly of deep x-ray, radium, potassium iodide and a minimal amount of surgery. During this treatment very little benefit was noted. Three cases have had a rather incomplete follow-up, however, the lesions were under control when last seen. The other cases—twelve—have been cured for as long as ten years.

The earliest case in this series was diagnosed and operated upon by Dr. George Eitel. The lesion was small and located on the right side of the neck. The duration of illness was five weeks and was treated by complete excision with an endotherm knife. The diagnosis was made after operation by study of paraffin sections taken from the exudate within the inflammatory mass. There has been no recurrence.

In each case we have listed the type of treatment followed. In some cases only one thorough surgical procedure was necessary, however, in others several operations were carried out.

#### SUMMARY

In the treatment of actinomycosis, if possible, complete eradication of the

diseased process by certain surgical procedures should constitute the chief therapeutic measure.

Wangensteen has very adequately stated the problem, "It is highly important, therefore, that actinomycotic wounds be frequently and meticulously examined. When a pocket has been well curetted, persistent drainage usually means an adjacent focus. The main consideration of most consequence is whether all the actinomycotic debris has been curetted away."

For supportive measures, potassium iodide and irradiation therapy are of value, but they should be considered of secondary importance.

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# PROLAPSE OF THE RECTUM

## A SUGGESTED OPERATIVE PROCEDURE FOR CURE

ISIDORE COHN, M.D.

Chief of Surgical Staff, Touro Infirmary

NEW ORLEANS, LOUISIANA

SUGGESTED innovations indicate dissatisfaction. For prolapse of the rectum a wide variety of procedures have been tried. Multiplicity of methods indicate diversity of opinion as to causative factors. Three main theories of origin have been offered: Esmarch suggested that the condition was due to an inflammation of the mucous membrane of the rectum. Jeannel suggested ptosis of the small intestines, which allowed them to sink in the cul-de-sac and by their weight cause pressure atrophy of the levator ani which ultimately gives way and allows prolapse. The third theory is that prolapse of the rectum is a hernia.

In 1912, Alexis Moschowitz after careful anatomic studies stated: "Prolapse of the rectum is a hernia and in all of its features it conforms to the well recognized principles of hernia-in other parts of the body." Moschowitz gives credit to Waldeyer, Ludloff, Napalkow, Dix and others for having done the original anatomic studies on which the hernia theory rests.

Moschowitz reminds us: "(1) The entire abdominal parietes are lined by peritoneum. (2) External to the peritoneum there is everywhere a layer of fascia. This fascia has received different names in different parts of the body, that is, the transversalis, pelvic, iliac, diaphragmatic, and etc. If traced it will be found that these are merely parts of one continuous layer. (3) All large vessels in the abdomen and all of the viscera of the abdomen lie upon the transversalis fascia and are covered by the peritoneum."

Moschowitz states further that, "A little reflection will show that hernias occur only where blood vessels or viscera make their

exit normally. In other words it is very apparent that these weak anatomic points must be attenuated peri-vascular or peri-visceral projections of the transversalis fascia."

This point is well illustrated by dia-grammatic representations included in Moschowitz's classic paper.

In considering the development of prolapse of the rectum if one accepts the sliding hernia theory of prolapse, one must keep in mind certain fundamental anatomic facts which have been so carefully pointed out by Moschowitz, they are: "(1) The peritoneum covering the anterior surface of the rectum is intimately adherent to it. (2) The undersurface of the levator ani is covered by a very dense fascia. Under normal conditions this fascia together with other component parts of the perineal body prevent the progress of the hernia in a downward direction for a time."

Any procedures which attempt to cure a prolapse of the rectum should fulfill certain indications: (1) Resection of the prolapsed bowel, (2) suspension and fixation of the bowel, and (3) repair and restoration of the pelvic floor.

The above indications are not met by many operative procedures which have been suggested. Practically all operations which are done transperitoneally take into consideration only one of these indications, that is, suspension and fixation of the sigmoid. Sigmoidopexy alone does not in anyway repair the pelvic floor. The latest procedure of this type was suggested by Pemberton in 1938.

"It was reasoned that if the pelvic colon could be pulled up until the rectum was taut and held in this position, at least tem-

porarily by sigmoidopexy, the rectum would become fixed in this taut position by the formation of scar tissue in the hollow of the sacrum and rectal prolapse thereby could be cured." (Pemberton.)

#### COMMENT

In this operation and like operations, no attention is paid to the weakness in the pelvic fascia and the possible prolongation of the peritoneal reflection of the cul-de-sac of Douglas through which a subsequent hernia could recur, whether or not a prolapse of the rectum did occur.

Operations in which the prolapsed rectum has been removed either by ligatures or ecraseurs, or even in which the prolapsed segment has been removed and the outer and inner cylinders sutured together at the line of section, fail to take into consideration the danger of injury to possible contents of the cul-de-sac. These operations also fail to consider the weakness of the pelvic floor.

As early as 1900, Ott recognized the importance of strengthening the natural support of the rectum. Ott, according to Moschowitz, performed "what is practically an inverted perineal plastic."

Napalkow was the first to recognize the importance of deep structures. He made a transverse incision in front of the anus, and worked his way upward to the peritoneum; this he closed off and finally sutured the two levators together.

Moschowitz objected to Napalkow's operation as he thought "it exceedingly difficult if not impossible to suture together at such great depths the two levators and the upper layer of the pelvis fascia with the requisite care and exactness."

In 1925, Maes and Rives recognizing the importance of the deep structures and the necessity for repair of the pelvic structures, suggested and carried into effect an operation in which they approximated the levators and supported the rectum by deep sutures. They give credit to Duval and Lenormont for having performed the operation in 1904, but their work was

independent of and without knowledge of the work of Duval and Lenormont.

The procedure which is here suggested is a composite operation. I have no illusion that the operation which is suggested and which we have used with success is by any means the final answer to a problem so difficult and which has occupied the attention of so many surgeons. It does, however, comply with certain fundamental principles.

In approaching the problem of the operative cure of prolapse of the rectum one must have a clear picture of the pathological anatomy. One of the clearest descriptions of complete prolapse is to be found in the chapter in Maingot's Surgery written by Ernest Miles:

"Pathological Anatomy—In those instances in which the whole of the rectum has been extruded, the tumor consists of a double tube, one placed within the other. The outer tube consists of the rectum, the mucosa being continuous with the skin of the anal margin at the base and with the mucosa of the pelvic colon at the apex of the protrusion. The inner tube consists of an equal length or more of the pelvic colon which has also been extruded. Between the two tubes in a prolongation of the pelvic peritoneum which forms a pouch anteriorly and at the sides, but not posteriorly. In cases of pronounced visceroptosis coils of small intestine descend into the peritoneal pouch."

In addition to the above there must be some weakness if not an absolute diastasis of the perineal muscles. The operation which is proposed has been carried out only once.

#### CASE REPORT

T. B., age thirty-eight, a white male, stated that he had had a prolapse of the rectum for eleven years. He was operated in February, 1940, at another institution. The operation consisted of multiple cauterizations of the mucosa. The patient stated that he was no better. When examined he had incontinence of feces; there was no blood in the stool, but

he thought that the prolapse had gotten progressively worse.

On examination of the rectum we noted that

The detailed steps of the procedure are as follows: Spinal anesthesia was used. The lower bowel had been thoroughly cleansed prior to

FIG. 1.



FIG. 2.



FIG. 3.

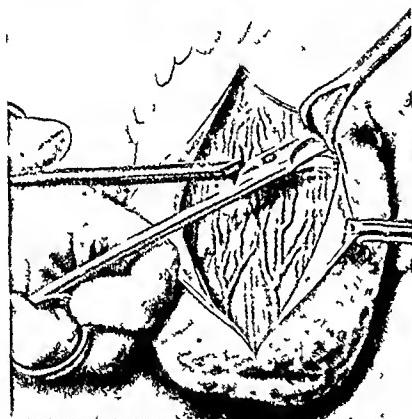


FIG. 4.

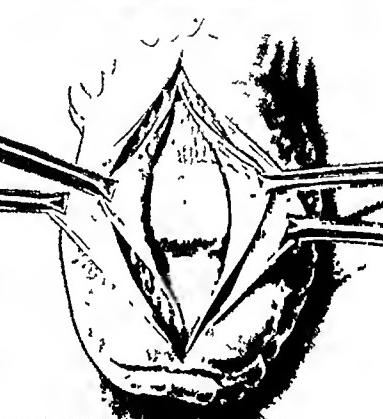


FIG. 1. Prolapse completely extruded.

FIG. 2. Incision in the long axis of the mucous membrane of the prolapsed bowel to within half an inch of mucocutaneous margin.

FIG. 3. Separation of mucosa from muscularis. Vessels on muscularis to be ligated.

FIG. 4. Incision through muscularis; the peritoneal pouch in the Douglas cul-de-sac is seen.

the anal orifice was wide admitting two fingers without difficulty. The sphincter was markedly relaxed. When the patient strained the prolapse could be seen extending about two and one-half to three inches beyond the mucocutaneous junction. Proctoscopic examination revealed apparently a normal mucous membrane without thickening.

The patient was admitted to Charity Hospital where he was operated upon.

When last seen November, 1941, five months after the operation, there was no evidence of prolapse and the patient had almost complete sphincteric control. At times there was some loss of control, in that he soiled his clothes, if the stools were liquid.

operation. At operation the patient was placed in the lithotomy position and the prolapse was completely extruded. A gauze strip was introduced through the lumen of the bowel as high as possible to avoid having continuous contamination of the field. On either side of the orifice of the bowel at the end of the extruded loop an Allis forcep was applied in order to give better fixation during the operative procedure. An incision was made in the long axis of the mucous membrane of the prolapsed bowel, the incision extended upward to within about one-half an inch of the mucocutaneous margin. The mucosa was retracted in order to expose the vessels and the muscularis of the everted loop. The vessels were clamped, ligated

and sectioned. The mucosa was separated from the muscularis circumferentially.

An incision was then made in the muscularis

ready for section or for use for traction purposes. The peritoneal opening was closed and a strip of gauze introduced so as to pack off the

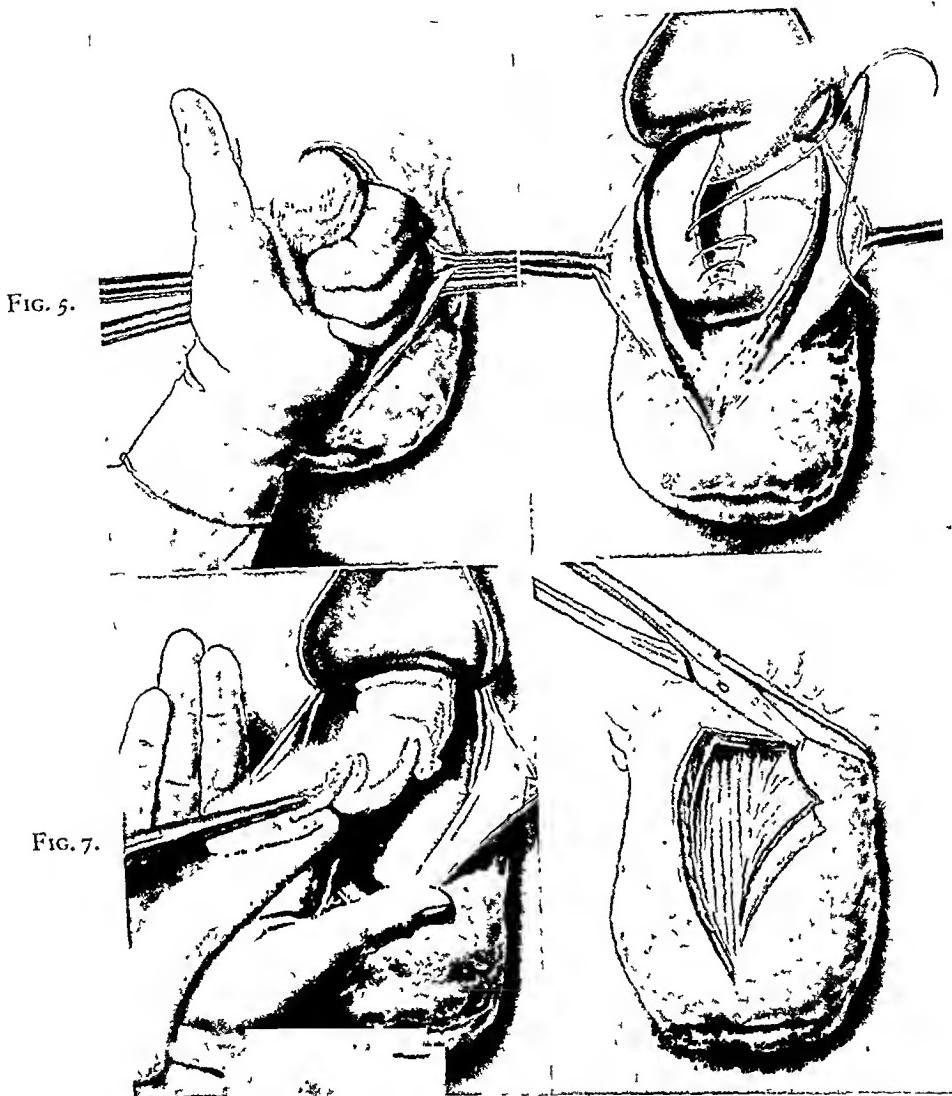


FIG. 5. Separation of bladder and peritoneal pouch from the rectum.

FIG. 6. The peritoneum has been opened and the bowel packed out of the way.

FIG. 7. Pack to hold herniated bowel and peritoneal reflection up during further stages of operation.

FIG. 8. Section of the muscularis and the outer coat of the everted loop.

of the everted loop and, after retraction of the incised muscularis and the outer coat of the loop, the peritoneal pouch in the prolonged Douglas cul-de-sac could be seen. The peritoneal pouch was separated from the rectum and the bladder by dry dissection. The peritoneum was then opened and the bowel was packed off. At this point the muscularis and the outer coat of the everted loop was sectioned near the mucocutaneous border just above what should be the sphincter. This then leaves the elongated barrel of the prolapsed bowel

peritoneal pouch. Gelpi retractors were introduced for exposure. Sutures were then introduced on either side into each of the levators and a bite of the outer surface of the rectal wall was included in the sutures. When the sutures in the levator had all been introduced they were tied one by one so as to fix the rectum at the highest point and also to repair the pelvic floor. The next step consisted in sectioning the proximal portion of the extruded loop. At this point a continuous suture or multiple sutures were used to approximate the cut end

FIG. 9.



FIG. 10.



FIG. 11.

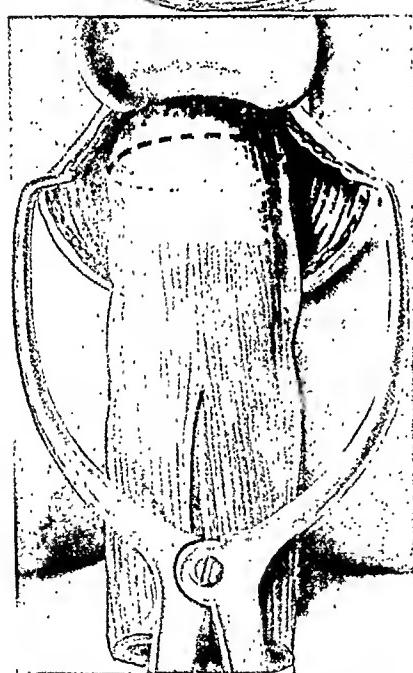


FIG. 12.



FIG. 9. The elongated loop is shown.

FIG. 10. Sutures introduced into each side through the levators to form a buffer.

FIG. 11. Point of sections of the prolapsed loop.

FIG. 12. Suturing the distal end of the bowel to the skin circumferentially.

near the mucocutaneous junction and the cut end of the proximal loop of bowel. No pack was introduced into the anal orifice at the conclusion of the operation.

It was not thought necessary in the case under consideration to plicate the sphincter.

#### SUMMARY

The operation as performed combined the features of many procedures which have been done singly before, but so far as I know the combined procedure has not been recorded in the literature.

I have no illusion that this is a final word; it simply represents certain steps which seem logical from an anatomic standpoint.

In hernias everywhere else the peritoneal pouch is considered, why not here? In hernias everywhere else the weakness in the

transversalis fascia or pelvic fascia is repaired, why not here?

This is a preliminary report and is offered with the hope that others may try the procedure and be able to aid in evaluating it.

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ALTHOUGH we occasionally see patients with procidentia who are nullipara, that does not detract from the indictment that practically all patients who exhibit procidentia have been neglected to a superlative degree.

# ACUTE SPINAL CORD COMPRESSION FOLLOWING HEMORRHAGE WITHIN EXTRADURAL NEOPLASM\*

REPORT OF TWO CASES WITH RECOVERY

LIEUT. COMDR. ABRAHAM KAPLAN, M.D.

U. S. Naval Hospital

PORPSMOUTH, VIRGINIA

THE signs and symptoms of a spinal cord neoplasm bear a direct relationship to the degree and rapidity of spinal cord compression. The occurrence of cord compression may be so slow and intermittent as to give rise to only mild and transient symptoms. Careful neurological study may yield no abnormal findings. Indeed it is well known that a patient may harbor a benign spinal cord neoplasm for years and give no evidence of any objective dysfunction. Often such patients are suspected of having a variety of ailments until compression of the cord brings forth the true nature of the disease. Certainly it is rather fortunate that at least 85 per cent of spinal cord neoplasms are very slow growing, benign and operable. These offer ample opportunity for early diagnosis. Our experience during the past decade shows a growing consciousness of the frequency of spinal cord tumors and so many more are being recognized during the phase of spinal cord dysfunction before permanent and extensive degeneration has taken place. The earlier recognition of these benign tumors has made our task of their removal much easier and the results have been more gratifying.

However, when we are confronted with acute compression of the spinal cord, whether due to external violence, an extradural abscess or a rapidly expanding neoplasm, we must realize that we are facing an acute surgical emergency. The reserve and resisting mechanisms of the spinal cord are easily overcome, and destructive processes, chiefly due to vascular disturbances and anoxia, set in early and progress rapidly.

Under these conditions the degree of functional return of the spinal cord will depend not only upon the underlying pathological disorder, but also upon the prompt recognition of the acute spinal cord compression, the correct level of compression and on the early surgical intervention. Acute spinal cord compression is frequently due to metastatic or malignant disease, but it may follow, as was recently pointed out by Eaton and Craig,<sup>1</sup> the removal of spinal fluid which precipitates a downward herniation of a spinal cord tumor, or it may be due to a hemorrhage within a benign extramedullary neoplasm. At any rate, no time must be lost in arriving at a course of action, and if surgery is decided upon there should be no delay.

## LITERATURE

In reviewing the problem of acute spinal cord compression as a result of hemorrhage within a spinal cord neoplasm, it is of interest to note that hemangiomas within or adjacent to the brain or spinal cord are not infrequently associated with nevi in the same dermatome. In 1906, Cushing<sup>2</sup> reported cases of spontaneous intracranial hemorrhage associated with trigeminal nevi.

Cobb,<sup>3</sup> in 1915, presented evidence to support the belief that hemangiomas are congenital and arise from developmental faults in the central nervous system and may similarly involve other organs innervated by filaments from that neuromere.

In 1927, Rand<sup>4</sup> reported two cases of hemangioma of the cord in association with

\* From the Neurosurgical Service of Mt. Sinai Hospital, New York City.

skin nevi in the somatic segment where the cord was being compressed.

In 1934, the author<sup>5</sup> reported a case of epidural hemangio-endothelioma in a patient who, in addition to many cafe-au-lait blotches over the body showed a large purplish elevated skin hemangioma measuring 10 by 15 cm. to the left of the spine which corresponded to the neuromere of the neoplasm. (Fig. 1.) The patient made a complete recovery and is well today.

Two years later, Buckley<sup>6</sup> reported the sudden onset of a flaccid paraplegia in a patient who subsequently was proved to have a hematomyelia secondary to a hemangioma.

More recently Johnson,<sup>7</sup> in 1938, reported an interesting case of an epidural hemangioma compressing the cord which went unrecognized for five years after the sudden onset of symptoms. Autopsy showed an epidural neoplasm with thin wall vessels and evidence of rupture and hemorrhage which undoubtedly was responsible for the sudden compression of the cord.

To Karshner, Rand and Reeves<sup>8</sup> must be given due credit as the first to diagnose preoperatively an epidural hemangioma producing acute spinal cord compression. In addition to scattered pigmented hemangiomatous nevi, their patient also showed x-ray evidence of a hemangioma of the vertebra. Microscopic study of the tissue removed at operation revealed evidence of recent bleeding within the endothelial channels of the tumor.

These authors stress the view that the presence of skin nevi in the same or adjacent skin segments of cord compression should promptly arouse the suspicion of a hemangiomatous lesion for which adequate preparation should be made before operation is undertaken.

Although the two cases to be reported did not show skin nevi, they nevertheless presented the syndrome of acute spinal cord compression due to hemorrhage within a benign neoplasm. It is the purpose of this communication to re-emphasize the syndrome of acute spinal cord compression and

to urge prompt surgical intervention before irreversible damage to the cord has taken place.

#### CASE REPORTS

**CASE 1.** On February 6, 1940, Grace H., a school teacher, aged twenty-two, was admitted to Mt. Sinai Hospital complaining of paralysis of both legs. On December 12, 1939, the patient slipped in the bathroom and fell heavily, striking the lower end of the spine. For a week following the injury she felt reasonably well, but then began to experience pain over the upper thoracic spines radiating forward in girdle fashion to both breasts. The pain gradually became more intense and was particularly distressing with motion, coughing or sneezing. In January, 1940, she went to bed, and with bed rest the pains lessened. On January 12, 1940, x-ray films of the spine were reported negative, and she was given a girdle for support.

Twelve days before admission diathermy treatments were started, and after three treatments the pain across the back almost completely subsided. About this time a numbness and heaviness of both legs set in, and at times both legs would suddenly jump up. Weakness of the legs progressed steadily and walking became more difficult, so that four days before admission she no longer could leave the bed. Simultaneously, the impaired sensation of the lower extremities advanced and spread to the midthorax. The loss of sensation soon became complete and the patient felt as if she were cut in half. For sixteen hours before admission she was unable to void.

Examination showed a very pleasant and co-operative young woman, whose general physical examination was negative. The positive neurological findings were as follows: (1) Spastic paraplegia of both legs, (2) diminution of pain and temperature sensibility between thoracic four and nine skin segments, and marked hypalgesia below thoracic nine skin segment. Light touch and position sense, however, were preserved and deep pressure sense remained intact. (3) The abdominal responses could not be elicited, knee jerks and ankle jerks were hyperactive and equal, Babinski sign as well as ankle clonus were present on both sides. (4) Spinal tenderness was most acute over the second and third thoracic spines.

X-ray films of the spine were negative. The manometric test showed complete block, the

spinal fluid was xanthochromic, and total protein was 104 mg. per cent.

Operation was performed on February 7,

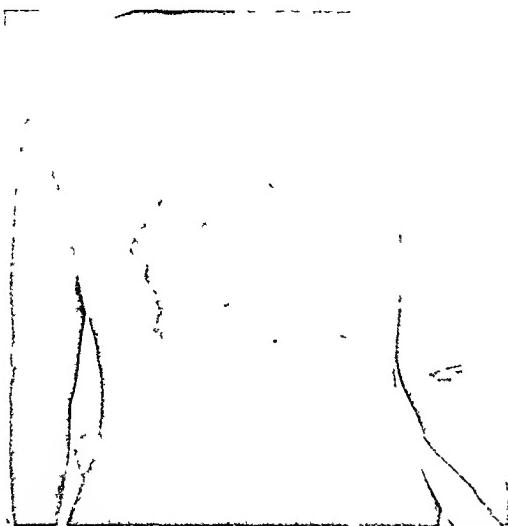


FIG. 1. Port-wine hemangioma in the neuromere corresponding to the extradural hemangioma. Note the cafe-au-lait blotch of the left forearm.

1940. A vertical incision was made from the second to the fourth thoracic spine. It was immediately noted that the skin, fascia and muscles were unusually vascular, with vessels of large caliber to either side of the spine. A transfusion was arranged for instantly. As the muscles were retracted tumor tissue was identified perforating through the second thoracic lamina on the left. After removing the spines and laminae from thoracic two to four, a well demarcated, fleshy, reddish brown tumor, measuring 4 cm. in length, was clearly visualized. The tumor bled freely from all surfaces but fortunately it was possible to separate the growth from the dura quite easily. After the complete removal of the tumor, the dura immediately began to pulsate normally and at this time a transfusion was started. After the bleeding was stilled, closure was carried out in layers without drainage. Gross inspection of the tumor showed a hemorrhage within its substance.

Microscopic section of the tissue revealed one area which was very cellular, consisting of closely packed cells with hyalin cytoplasm and elongated darkly staining nuclei. The nuclei varied considerably in shape, and in places were arranged in cord-like masses. (Fig. 2.) There were also many giant cells, some containing as many as twenty nuclei which had no consistent distribution. (Fig. 3.) The tissue was

abundantly supplied with vessels. In another portion of the tumor there were many large broken down vascular spaces with hyalinized concentrically arranged arterioles showing endothelial proliferation. Areas of hemosiderin were not infrequent in this region. (Fig. 4.) There were no mitotic figures.

Diagnosis: Giant cell tumor.

On the morning after the operation the patient stated she felt that her legs again belonged to her. On the third postoperative day the spinal fluid was xanthochromic and manometric test showed a slow rise and fall upon jugular compression.\* One week after operation she voided spontaneously. The wound healed by primary union. Manometric test on the eleventh postoperative day showed a prompt rise and fall upon jugular compression. The spinal fluid was clear and colorless.

It was interesting to note the manner in which function returned. At first there was a feeling that the legs belonged to the body. Pain and temperature were first experienced more acutely in the lower portion of the legs. Power in the vasti medialis and lateralis manifested itself first in the right leg, then in the left. The internal rotators began to function before the external rotators. Movement in the toes was a later manifestation.

A month after the operation she walked with moderate assistance. She was able to abduct and raise both legs with ease. Babinski sign was no longer present. From then on improvement in sensation and power was steady, but not as rapid. She was given 800 roentgen ray units over the operative site as a prophylactic measure.

At the time of discharge on April 6, 1940, sensation was normal, gait was slightly spastic, there were no pathological reflexes and sphincter control was excellent.

Now over one year since the operation she is in excellent health, walks very well and is at her job as a music teacher.

\* For the past seven years it has been our practice to make certain that subarachnoid block is completely relieved after the removal of a spinal cord tumor. On several occasions partial or complete spinal manometric block was found on the third or fourth day after operation, but a repetition of the manometric test several days later consistently showed an open subarachnoid system. Our explanation for this temporary block has been that it was due to edema of the tissues at the operative site. Should block of the subarachnoid space persist after a fortnight, the patient should be investigated further for some additional cause of subarachnoid obstruction.

## COMMENT

Giant-cell tumors of the vertebrae are not uncommon as can be readily learned

These tumors may eventually cause collapse of a vertebra or a break through into the subdural space resulting in spinal



FIG. 2.

FIG. 3.

FIG. 4.

FIG. 2. Case 1. Arrangement of elongated dark staining nuclei in vicinity of giant cells.

FIG. 3. Case 1. Typical giant cell with nuclei centrally placed.

FIG. 4. Case 1. Hemosiderin, shown in dark areas, is evidence of previous hemorrhage within neoplasm.

from the reports of Lewis,<sup>9</sup> Duncan and Ferguson,<sup>10</sup> Pierce and Lampe,<sup>11</sup> and Willard and Nicholson.<sup>12</sup>

cord compression. However, in this patient repeated x-ray studies of the vertebrae and microscopic study of the bone removed at

operation failed to show any evidence of giant-cell tumor involvement. Gross and microscopic evidence leaves no doubt of a

Inquiry into dietary habits readily disclosed that there was a serious deficiency in the consumption of fresh vegetables, eggs and other

FIG. 5.

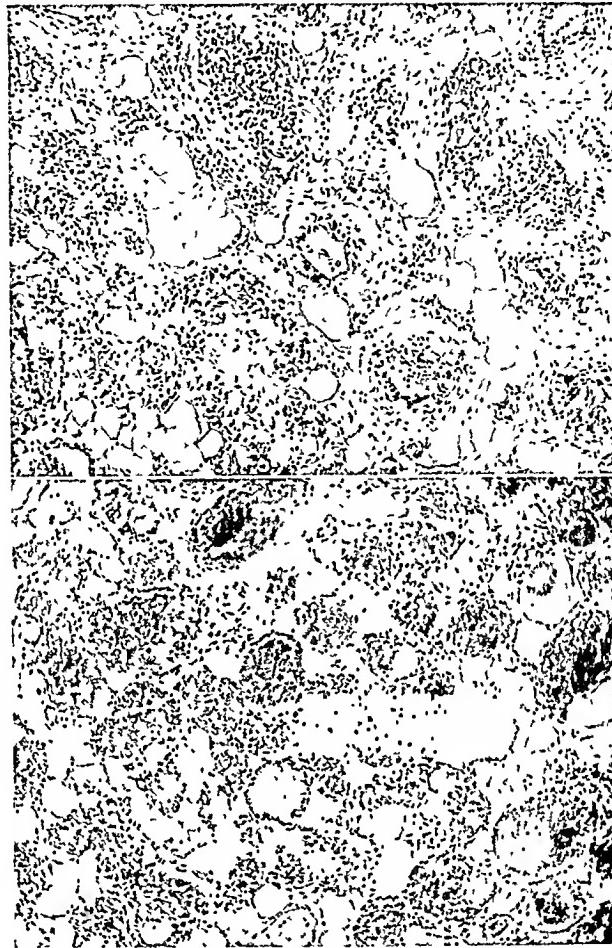


FIG. 6.

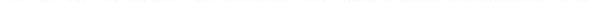


FIG. 5. Case II. Cavernomatous channels with thin, frail walls.

FIG. 6. Case II. Vascular spaces engorged with red blood cells showing evidence of endothelial rupture.

hemorrhage within the neoplasm. The determining factors which were responsible for this speedy and complete functional recovery were the prompt recognition of the acute spinal cord compression and the immediate surgical intervention. A series of deep x-ray therapy over the involved spine was given because of its known beneficial influence on this type of neoplasm in the event that some cells may have been left behind.

CASE II. Yetta R., aged forty-four, was admitted to Mt. Sinai Hospital on January 9, 1940, because of weakness and inability to walk.

vitamin B<sub>1</sub> foods. Nevertheless, she was apparently well until five weeks before admission, when she began to experience a dull pain across the lower thoracic spine, which was aggravated when lying down.

For three weeks her diet consisted only of milk and water. The pain continued until about one week before admission, when she felt a constriction band about the lower thorax, and two days later she suddenly noted numbness in the toes of the left foot. She felt faint and dizzy. The back pain disappeared. On the following day the numbness spread to involve the toes of the right foot and rapidly ascended up both legs and to the subcostal region. The legs became weak, gait was unsteady and she

had to remain in bed. She soon found difficulty in voiding.

At examination the patient appeared thin, dehydrated, anxious and pale. The description, "a cachectic appearance," fitted her well. Heart and lungs revealed no abnormality. Blood pressure systolic 150, diastolic 90. On palpation a large, firm, smooth movable mass was found filling the entire left side of the abdomen, extending upward to about 3 em. above the umbilicus. The uterus was irregularly enlarged by a fixed mass arising in the pelvis and extending upward to join the abdominal mass. The adnexa could not be differentiated from the mass.

Neurological examination showed (1) marked weakness and moderate atrophy of both legs. (2) There was a zone of hyperalgesia at thoracic 6 skin level which corresponded with the subjective girdle pains. (3) Below thoracic 7 dermatome there was loss of pain and temperature sense as well as of two point discrimination. Vibration sense was diminished below the ankles. (4) There was sacral sparing to pain and light touch. (5) Both knee jerks could not be elicited. There was acute spine tenderness over thoracic 5 and 7 spines.

X-ray films of the spine showed slight spondylitis of the lower thoracic spine and slight convexity to the right in the midthoracic area. Hemoglobin 50 per cent, red blood cells 4,500,000 per cu. mm., leucocytes 6,650 per cu. mm. Blood Wassermann test was negative. Lumbar puncture showed an initial pressure of 68 mm. of water; there was no rise upon jugular compression, although abdominal compression caused a prompt rise and fall. The spinal fluid was clear and colorless, Pandy 4 plus, 7 mononuclear cells, Wassermann reaction was negative, and total protein 135 mg. per ecnt.

It was no easy matter to decide whether we were dealing with a metastatic neoplasm to the spine or two independent tumors. The patient's general condition did not promise an encouraging outcome, nevertheless it was decided that the spinal cord compression was most urgent and could least afford any surgical delay.

Operation was performed January 12, 1940. The patient was given a general anesthetic and before placing the patient in the usual laminectomy position, the operating table was built up so as not to cause undue pressure upon the

abdominal mass. A blood transfusion was started. Incision was made from the third to the sixth thoracic spines. There was generalized bleeding from the skin, fascia and muscles, and much of the bleeding could only be controlled with hot packing. When the spine and laminae of the fourth thoracic vertebra were removed, a red, fleshy, hemorrhagic, friable extradural tumor came into view. Further bone removal was necessary to expose the limits of the tumor which extended from thoracic two to thoracic six and extended around laterally. A frozen section biopsy of the tumor was reported benign hemangioma. Fortunately, the tumor separated easily and cleanly from the dura and was completely removed. The wound was closed in layers in the usual manner without drainage.

Microscopic sections of the tumor (Fig. 5) showed many varying sized vascular channels often cavernomatous in character. The walls of the channels were lined with aggregations of round and elongated cells, and in places the walls appeared very thin and frail. In some areas the channel spaces were unusually large and engorged with red blood cells (Fig. 6), while in other portions of the tumor there is evidence of rupture of the endothelial lining with resulting hemorrhage.

#### Diagnosis: Hemangio-endothelioma.

Within a week postoperatively movements of the legs became more and more active. The power in the right leg returned more quickly than in the left. Pin prick and vibration were perceived sooner on the right. On the eighth postoperative day she voided spontaneously.

By the end of a fortnight she was out of bed, taking a few steps. A week later she was examined by Dr. I. C. Rubin, who believed that the removal of the abdominal mass was not urgent and that it was more desirable to permit a further period of improvement to elapse before operative intervention.

Neurological examination on the seventeenth postoperative day revealed complete disappearance of any objective abnormal sensory disturbances, though the patient was troubled with a variety of dysesthesias and paresthesias.

On March 5, 1940, a series of x-ray therapy was started as a prophylactic measure. A total of 1,200 roentgen units were given to each side of the operative site.

The patient was discharged on March 14, 1940, able to walk without assistance.

*Second Admission November 22, 1940.* Since her discharge the patient gained in general health as well as in power of both legs. The size of the abdominal tumor, however, remained unchanged.

On November 25, 1940, laparotomy was performed by Dr. I. C. Rubin, who found a massing of multiple fibromas of the uterus with three large fibroid tumor masses measuring 15 by 20 by 10 cm. In addition there was a large endometrial cyst of the left ovary. All were completely removed. The postoperative course was smooth and uneventful. On December 14, 1940, she was discharged in excellent health and to date is carrying on her household duties without any difficulty.

#### COMMENT

Schlesinger and Ungar<sup>13</sup> collected thirty-three proved cases of hemangioma of the vertebrae associated with neurological manifestations due to compression of the spinal cord. Of these there were only eight instances of epidural angiomas. Profuse bleeding was encountered in those patients who came to operation and was the direct cause of death in many instances.

In our patient there was no x-ray evidence of a hemangioma of the vertebrae. Instead, we had strong suspicions of a metastatic malignancy to the spine. Transfusion was started before the operation was actually begun. The bleeding encountered at the operation was indeed troublesome, and was due in part to the increased vascularity of the tissues surrounding the tumor. However, when the frozen section biopsy was reported as a benign hemangioma, the neoplasm was attacked with greater vigor and fortunately was completely removed before the patient started to show the effects of blood loss. The series of x-ray treatments had a very beneficial effect upon any microscopic tumor cells which might have been left behind.

The delay of ten months before the removal of the abdominal tumor as advised by Dr. I. C. Rubin greatly benefitted the patient. At the time of the second hospital

admission the patient's general health was excellent, so that in spite of the difficult removal of an unusually large and adherent tumor she made a smooth and splendid recovery.

#### SUMMARY AND CONCLUSIONS

Two cases of acute spinal cord compression, which benefitted by early surgery, are reported as evidence that this condition need not offer such a poor and unsatisfactory prognosis..

The acute spinal cord compression in each instance was due to a hemorrhage within a benign extradural neoplasm.

Emphasis is placed upon the early recognition of acute compression of the spinal cord and it is further advocated that such a condition should be treated as an acute surgical emergency.

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# A NEW SIGN TO DIFFERENTIATE ABDOMINAL MUSCULAR RIGIDITY IN CASES OF ACUTE ABDOMINAL CONDITIONS FROM THAT OF OTHER CAUSES

ARNALDO YODICE, M.D.

Assistant Professor de la Facultad de Ciencias Médicas

BUENOS AIRES, ARGENTINA

**A**GREAT deal of experience in emergency surgery has enabled me to study a new maneuver which gives important data in certain cases of acute conditions of and painful abdomen in which the diagnosis cannot be established by other means. In the great majority of the cases, such as appendicitis, perforated ulcer, acute cholecystitis, etc., the patient presents a clear symptomatology with pain on pressure and muscular rigidity over the site of the lesion.

The contraction of the abdominal wall is a reflex from abdominal pain arising from a peritoneal reaction or from some type of colic, such as intestinal, ureteral, kidney, hepatic duct, common duct or gallbladder. Nevertheless, at times one observes patients who present contractions of the muscles of the abdominal wall (muscle defense reaction) with generalized mild or acute pain, and in these cases interpretation of the signs is extremely difficult. If the symptomatology of these painful attacks is not typical, the surgeon is dealing with a therapeutic problem which is very difficult to solve. It is a question whether the signs are due to an acute condition of the abdomen with a muscular defense reaction induced by peritoneal inflammation (peritonitis), or whether it is the result of a defense reaction arising from other causes such as pain of a colicky type without inflammation of the peritoneum. The following maneuver serves to establish the differential diagnosis between the muscular contraction from peritoneal reactions and those from other causes.

The palpation is done in the following manner: The patient is placed in the dorsal

decubital position with the thighs abducted and flexed to 90 degrees, and the feet resting on the bed or examining table. The index and middle fingers are introduced into the rectum to dilate the anal sphincter. At the same time, the left hand palpates the abdomen at the site of the muscular contraction.

## INTERPRETATION

If at the moment that the dilatation of the anal sphincter is accomplished the muscular contraction of the abdomen *does not disappear*, it is a positive sign and denotes that the muscular contraction is due to peritoneal irritation (peritonitis). If during the introduction of the fingers which dilate the anal sphincter, the muscular contraction *disappears*, it is a negative sign and signifies that the contraction is due to pain of a colicky type whose treatment is not an emergency surgical procedure. The maneuver may be repeated many times until one attains a clear interpretation.

This sign serves to establish the differential diagnosis between the following syndromes: (1) Muscular contraction of the abdomen of inflammatory origin due to peritoneal infection (peritonitis), and a contraction produced by pain of a colicky type (intestinal, ureteral, hepatic gallbladder, uterine, etc.). (2) Muscular contraction from peritoneal infection (peritonitis) and contraction of nervous origin induced by irritation of the nerves of the spinal column or periphery. The latter includes peripheral neuritis, wounds from firearms or trauma of the spine. In these last cases, especially in the wounds by firearms, the

patient presents muscular contraction of the abdominal wall, in which case it is necessary to establish the diagnosis between intestinal perforation (defense reaction from peritonitis or peritoneal irritation) and reflex contracture from lesions of the nervous system (medulla or nerves). (3) Cases of "phantom" tumor produced by contraction of the abdominal wall or intestine, and of true tumor the result of neoplasm or new growth. When a phantom tumor is present, it disappears during the dilatation of the sphincter of the anus (negative sign).

Valuable information is also obtained by this test in cases of retroperitoneal tumor, aoritis, or aneurysm of the abdominal aorta in which at times there is a muscular contraction of the abdominal wall. In cases of aortic aneurysm, the pulsation becomes less marked, and the muscular contraction disappears at the moment the anal sphincter is dilated. The tumor diminishes in size.

Before applying this maneuver, we tried many diverse procedures to obtain a distant reflex after distracting the attention of the patient, but the results were not constant. For example, we produced sensations by pinching the skin of the arm, pricking with a needle, and applying tubes of hot and cold water to different parts of the body without observing variations in the contracture of the abdominal wall. Moreover, when one applies these sensa-

tions near the skin of the abdomen, the contracture increases. Pathological conditions in the neighborhood of the anal sphincter may evoke many distant reflexes, and we have observed distant disturbances provoked by fissures in ano which, in some cases, cause syncope. Evidently, the dilatation of the anal sphincter produces spinal and sympathetic reflexes which modify the muscular contraction of the abdominal wall. If the reflex is intense, as is seen in those cases with peritoneal irritation, dilatation of the anal sphincter is incapable of interrupting the reflex arc.

#### CONCLUSION

A new sign for the differential diagnosis of muscular contraction of the abdomen caused by peritonitis or peritoneal irritation and of reflex contractions produced by pain of a colicky type or irritative lesions of the nervous system has been described. The sign also establishes the differential diagnosis of phantom tumors (abdominal aortitis) and true tumors of the abdominal wall, the intestine or the retroperitoneal tissues.

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# CONTINUOUS CAUDAL ANESTHESIA IN OBSTETRICS\*

WALDO B. EDWARDS, M.D.

AND

ROBERT A. HINGSON, M.D.

Passed Assistant Surgeon, United States Public Health Service, U. S. Marine Hospital

STAPLETON, STATEN ISLAND, NEW YORK

CONTINUOUS caudal anesthesia, or the extradural introduction of fractional doses of anesthetic substances through the sacral hiatus into the sacral canal, has been practiced by us at the U. S. Marine Hospital, Stapleton, Staten Island, New York since early January, 1942. We consider this form of anesthesia to be an improvement over the conventional type of peridural anesthetic administered by a single injection. In this latter procedure the time limit of satisfactory anesthesia is from forty-five minutes to two and a half hours, while with continuous caudal administration, the anesthesia can be safely prolonged indefinitely. The maximum time of effective anesthesia during labor, in our experience, has been thirteen hours.

During 1941, we were impressed with the anesthesia produced by a single peridural injection into the lumbar area and in the sacral canal of 2 per cent metycaine in a series of thirty obstetrical deliveries and two hundred surgical procedures. We found this single injection method of peridural anesthesia to be very satisfactory for delivery after complete cervical dilatation, but we sought to develop a procedure that would relieve the parturient of that distressing and exhausting experience throughout the early stages of labor.

After Lemmon's<sup>1</sup> contribution in 1940 of continuous spinal anesthesia, we decided to combine the advantages of the continuous method with the safety, simplicity and effectiveness of the extradural nerve block by using the sacral hiatus approach to the sacral canal and the peridural space.

To date we have used continuous caudal anesthesia for obstetrical delivery in thirty-three cases. Of this number, six were multiparae and twenty-seven were primiparae. In all of these cases there was complete eradication of all the pain and discomfort of active labor within five minutes after administration of the anesthetic. In every case there was immediate and complete relaxation of the cervix and the pelvic floor which expedited the progress of labor without interfering with uterine contractions.

Since most of these patients were primiparae, episiotomy and outlet forceps were used in twenty-three cases to facilitate the lifting of the head over the perineum. In ten of these cases the labor progressed so smoothly that the use of forceps was not necessary. Under this form of anesthesia, these patients were entirely free from pain during these procedures. Likewise the repair of the episiotomy produced no pain.

There was spontaneous respiration of the infant following delivery in every case except one with no form of resuscitation necessary. The one exception mentioned was the delivery of a still-born infant in which fetal death had been determined several days before delivery. After the administration of the anesthetic, the parturients are mentally and physically at ease and are able to bring to bear all of the voluntary expulsive forces to co-operate completely with the accoucheur. The symptoms of delirium, narcosis, cyanosis, nausea, vomiting and anoxemia so often seen with other forms of anesthesia are uniformly absent in these cases. This substantiates a recent plea of DeLee in which he states: "I find a local anesthetic can be used a

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great many more times than it has been used, and it shows a decreased mortality and morbidity statistics. It stands to

established that the uterus derives its extrinsic nerve supply from three sources, i.e., the motor fibers to the uterus are

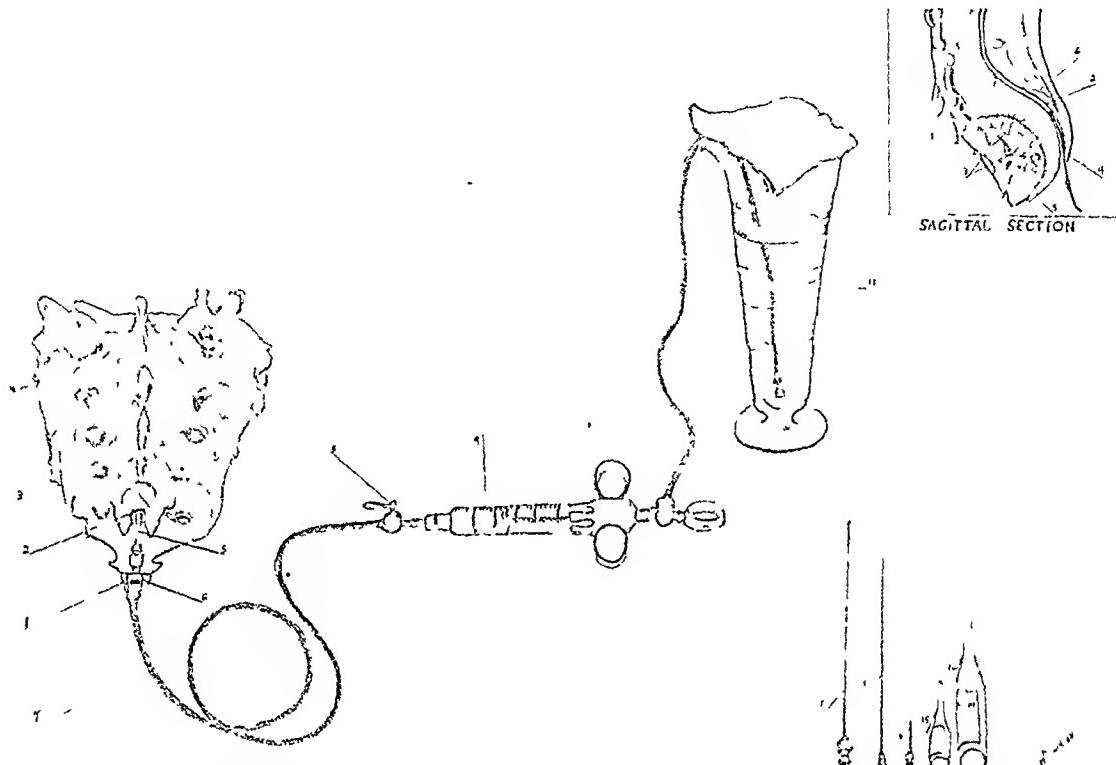


FIG. 1. Apparatus needed for continuous caudal anesthesia. Key to drawing: 1, coccyx; 2, saeral hiatus (entrance to sacral canal); 3, posterior sacral foramen; 4, sacral articulation with ilium; 5, Lemmon flexible silver spinal needle in place within the peridural space of the sacral canal; 6, Luer-lok connector; 7, rigid rubber tubing of the Lemmon continuous spinal set; 8, control valve; 9, continuous flow Pitkin 5 cc. syringe; 10, connecting tube between syringe and sinker strainer in bottom of graduate; 11, 125 cc. graduate containing 1.5 per cent solution of metycaine in physiological saline; 12, extra flexible silver needle (Lemmon); 13, stilet for flexible silver needle; 14, skin wheal needle; 15, ampoule 1:2600 adrenalin; 16, ampoule containing 5 cc. of 20 per cent metycaine for dilution with physiological saline. Sagittal Section: 1, corpora of sacral vertebra making up floor of sacral canal; 2, sacral spine and lamina making up roof of sacral canal; 3, anterior nerve roots of the sacral plexus; 4, sacral hiatus with needle in situ; 5, distal vertebra of coccyx; 6, sacral canal.

reason that you should anesthetize only the part of the body that is being operated upon. Why put the whole body under anesthesia when you are going to operate on one part? There are three reasons for local and regional anesthesia; first, its availability; second, its safety from complications; and third, the after results."

The approach to the problem of the control of pain in childbirth should follow the pathway of a study of the fundamental anatomy of that portion of the maternal organism concerned in the mechanism of labor. The classical work of Cleland<sup>2</sup>

derived from the sympathetic nerves of the aortic plexus reinforced by fibers from solar, renal and genital ganglia; the sensory fibers to the uterus are derived from sympathetic nerves and ganglia of the eleventh and twelfth dorsal spinal segments; and the sensory fibers to the cervix, and also the birth canal, are found in the parasympathetic plexus of the sacral nerves. The perineum receives its nerve supply from the lower divisions of the sacral plexus of somatic nerves. All of these sensory nerves are blocked by a sacral peridural injection of a local anesthetic.

Cathelin, a French urologist, blocked the sacral and coccygeal nerves through the sacral hiatus. He found, in 1901, that fluids when injected into the peridural space by this route rise to a height in direct proportion to the amount of preparation used and the speed with which it was forced into the canal. He further showed that when sufficient cocaine was injected into the sacral canal of the dog, it resulted in complete anesthesia of the entire body.<sup>3</sup>

Laewen, Gaza and Schlimpert used caudal anesthesia in Germany in 1919 for obstetrical cases.<sup>4</sup> In America, the technic has been used successfully by Meeker and Bonar in 1923; others followed: Oldham in 1925, Lundy in 1928, Henry and Jaur in 1929, Rucker in 1930, Campbell in 1935, Johnson in 1936 and Sword in 1936.<sup>5</sup> In 1939, Baptisti reported the successful use of caudal anesthesia in 200 obstetrical cases.<sup>6</sup> Lahmann and Mietus in January, 1942, reported 400 obstetrical cases in which caudal anesthesia was used.<sup>7</sup>

These investigators confirm the practical usefulness of the method with comparative safety for both mother and child during labor. Most of them describe a satisfactory anesthesia resulting from an introduction of from 30 to 40 cc. of 1 or 2 per cent solution of novocaine or metycaine into the extradural space of the sacral canal. Most of them found the duration of this anesthesia to be between forty minutes to an hour and a half.

We have sought to modify their methods in such a way that the anesthesia could be started in the early stages of labor to relieve the pain and discomfort for the parturient in this period, yet, at the same time, we have continued this anesthesia for the prolonged length of time necessary to complete labor, and if necessary, to effect a repair of an episiotomy or laceration. Our series of cases has been small because of the limited size of the obstetrical service in the Marine Hospital.

The following table illustrates the number of hours each case enjoyed complete anesthesia during labor with dosage in

Gm. of 1 and  $\frac{1}{2}$  per cent metycaine consumed in fractional doses during this period. (Table 1.)

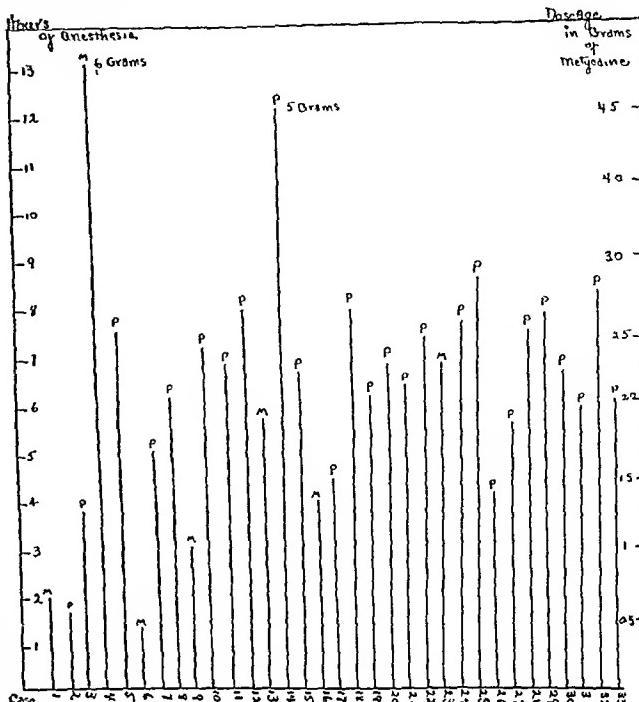


FIG. 2. As it can be determined from the chart, the average time of anesthesia for all cases was between six and seven hours. Many of the cases with shorter periods of anesthesia came to the hospital in the active stage of the latter part of labor. In most of the other cases the time that anesthetic was administered represented the entire course of labor. The symbol M indicates multiparae; the symbol P indicates the primiparae. The high percentage of primiparae is explained by the fact that most of the patients were young wives of officers and enlisted men in the Coast Guard.

From the table it can be seen that most of our patients received the anesthetic between five and six hours. For most of these this period represents the entire period of labor. It was found that a fractional dose of from 20 to 25 cc. of a 1 $\frac{1}{2}$  per cent solution of metycaine each hour was sufficient to relieve the pains and discomforts of labor.

The following is an outline of the technic used in this hospital:

#### TECHNIC

1. After the accoucher has made a thorough survey of the case and is convinced that the true labor pains of the first stage of labor have begun, the patient is

prepared for continuous caudal anesthesia. If the patient is a primiparae, and a labor of several hours is anticipated, the

skin wheal is raised below this point with the local anesthetic solution.

4. A sixteen gauge, Lemmon malleable

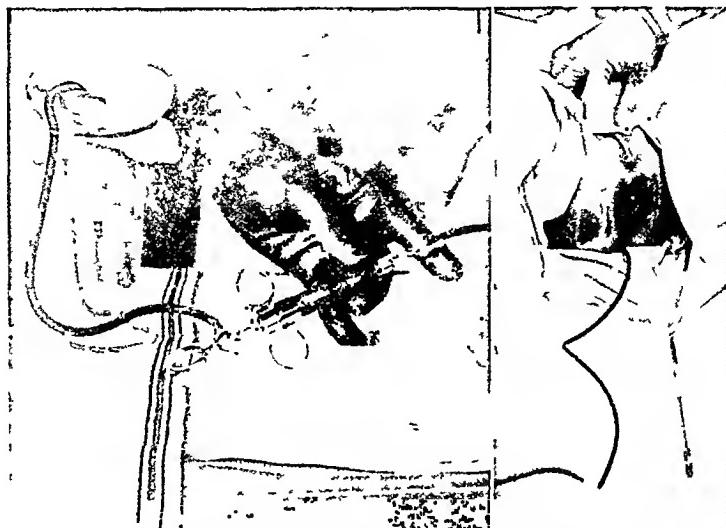


FIG. 3. Apparatus for continuous caudal anesthesia; flask containing 1½ per cent metycaine; Pitkin continuous flow 5 cc. syringe (Becton Dickinson); Lemmon semirigid rubber tubing with control valve.

anesthesia may be started with the patient in her hospital bed. Such a course may also be selected for the multipara in whom the accoucher has found dystocia or protracted labor.

Parturients who by their course and physical findings give indication of early deliveries are transferred immediately to the delivery room. We give no sedation such as barbiturates unless there is extreme nervous tension with anxiety on the part of the patient.

2. The administration of the anesthetic is performed with the patient in the knee-elbow or knee-chest position for the insertion of the caudal needle into sacral canal. It can also be administered with the patient on her side in the position of universal flexion as for spinal anesthesia.

3. The tip of the coccyx is palpated with the middle finger, and the thumb is used to find the inverted V-shaped notch of the sacral hiatus, which is usually about one and a half to two inches cephalad from the inferior caudal tip. The middle finger is then held in this notch as a guide, and a

FIG. 4. Parturient draped for delivery with continuous caudal tubing exposed for photographic purposes. Note relaxation of perineum and anus; spontaneous crowning five minutes before delivery.

silver\* spinal needle is then inserted through the skin wheal and through the sacral hiatus into the sacral canal until the needle comes to rest on the anterior bony wall of the canal. The needle should be inserted within the canal for a distance of about 5 to 7 cm.

5. The hub of the needle is then securely attached to the rigid rubber tubing of the Lemmon continuous spinal apparatus by means of a Luer lock connector.

6. An initial dose of 30 cc. of 1½ per cent metycaine solution in physiologic saline is injected into the sacral canal at an even speed in one minute. For this procedure we use a continuous flow 5 cc. syringe with a rubber tube inlet from a covered sterile graduated flask containing the anesthetic solution. In our experience

\* Pilling Company.

the parturient is free from pain within five minutes.

7. The hub of the caudal needle may be secured in the median raphe just caudal to the sacral hiatus by means of a small strip of adhesive tape which does not interfere with the antiseptic preparation of the patient.

8. With the anesthetist carefully transposing the connected tubes and syringe to a small Mayo stand just beside the delivery table, the patient is simultaneously permitted to turn on her back.

9. The parturient is now placed in the lithotomy position for the delivery of the baby. The perineum can be scrubbed with soap and water. The vulva and even the interior of the vaginal vault may be painted or sprayed with one of the antiseptic tinctures such as mercresin or merthiolate without discomfort to the patient.

10. The anesthesia can be continued indefinitely by serial injections of the anesthetic solution at intervals in amounts varying with individual cases. We have found that most of our patients are comfortable if 20 cc. of additional anesthetic solution is injected every thirty to forty minutes. The interval of the serial injections may be shortened, and the amounts increased if the patient should have any discomfort.

In our series of thirty-three deliveries, we used this form of anesthesia for a maximum of thirteen hours in one case, and twelve hours in another, for seven and a half hours in another case, and for an average of four and three-quarter hours in all cases. In none of these cases was the momentum of uterine contractions retarded. The perineum was relaxed from the onset, and the cervix seemed to dilate more rapidly with the anesthesia than without it. We believe that in all of our cases the entire labor was shortened by several hours. The deliveries of most of the primiparae occurred by elective use of outlet forceps and episiotomy. The deliveries of the multiparae occurred spontaneously.

There were no postoperative complications in any way related to the anesthetic. There were no unusual systemic reactions on the delivery table. Three patients were nauseated and vomited once, but for the remaining hours of labor felt comfortable. Several of the patients actually went to sleep after their pains had been relieved. Several expressed a desire for food or water. Both were administered in small quantities when requested.

One of our cases was in the midst of eclamptic convulsions when she was admitted to the hospital in the early stages of labor. Her blood pressure was 220/110. She was talking incoherently, and complained of blurred vision. Anesthesia was begun at 4 A.M. The patient immediately became comfortable; her blood pressure dropped to 140/90 and her blurred vision cleared remarkably. Her clinical picture was so remarkably improved that we continued the anesthesia throughout the day, during which time fifteen-minute checks of her blood pressure revealed that it did not at any time exceed 150. Because of the length of labor we increased the interval of administration of the serial doses. The parturient herself requested each of the serial doses. She delivered spontaneously a five-pound premature, but apparently healthy male infant thirteen hours later.

The following is the case report of another patient in our series illustrating the advantages of the method:

#### CASE REPORT

CASE VI. The parturient was a colored female, age twenty-one, primiparous, who had a substantiated case of syphilis by history, laboratory and clinical findings. Her husband had a positive serology. The patient was given regular antiluetic therapy from the twentieth to the thirty-seventh week of her pregnancy. At this time she developed symptoms of arsenical toxicity with evidence of hepatitis. Her renal function was not impaired and there was no elevation of her blood pressure. The patient was hospitalized and the antiluetic therapy discontinued.

Pelvic measurements and size of the fetus had been previously determined by x-ray, and no contraindication to delivery via the pelvic route had been found.

The patient went into spontaneous labor during the night and did not notify the nurse until she had a definite feeling of discomfort. On examination at this time it was determined that she had a 3 cm. dilatation of the cervix and that the fetus was in the left occipito-anterior position.

Continuous caudal anesthesia was started at this time according to the technic outlined. As the uterine contractions became stronger and more frequent in the latter part of the first stage and the early part of the second stage, the parturient was encouraged to bear down with her contractions. She had no discomfort and at times would fall asleep.

During the early part of the second stage of labor about four ounces of large luetic vulval condylomas were removed by cautery since these growths interfered with the relaxation of the perineal floor. Midforceps were then applied to facilitate extension of the head. After median episiotomy, the head was lifted over the perineum and a normal eight-pound male infant was delivered. The baby breathed spontaneously. The episiotomy was repaired without discomfort to the patient. The length of anesthesia had been seven and a half hours. The total amount of the metycaine was 160 cc. of 1½ per cent solution.

The blood pressure remained around 115 systolic and 80 diastolic. The systemic condition of the parturient was good. Her only discomfort, consisting of backache and stomach pain, occurred for ten minutes during cervical dilatation, one hour before the birth of the baby. Another routine serial injection of 20 cc. of the anesthetic relieved her.

The placenta was expressed easily and the amount of blood lost during delivery was estimated to be about 300 cc.

#### SUMMARY AND CONCLUSIONS

1. A new form of anesthesia in obstetrics is presented.

2. The advantage of this method, in which the distressing pains of early as well as late labor are alleviated, is emphasized. Likewise, the improvement of this form of anesthesia over the conventional single injection peridural anesthesia is indicated.

3. A short history of the steps leading up to this form of anesthesia from the literature is presented.

4. An outline of the technic for continuous caudal anesthesia is recorded.

5. The unusual features of the anesthesia with thirty-three obstetrical cases are presented.

6. A case report of a complicated delivery under this form of anesthesia lasting seven and a half hours is discussed.

We are continuing a study of this method. We realize that our series is too small to make all inclusive assertions as to its merit, but we do suggest that our small experience indicates the method is worthy of further study in the larger clinics in which an accurate evaluation can be obtained.

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# CONSERVATIVE OPERATIONS ON THE UTERUS

IRENE A. KOENEKE, M.D.

HALSTEAD, KANSAS

REMOVAL of the uterus during the child-bearing years is followed by a premature artificial menopause in from three to six months following hysterectomy unless sufficient endometrial tissue remains at the cervical stump to maintain ovarian function. This statement is made in full knowledge that no endometrial hormone has been discovered to date and that theoretically it should be possible to remove the uterus and ovarian function continue. In the field of animal experimentation the work of D. R. Mishell and L. Motyloff substantiates this stand. They reported ovarian atrophy in rabbits three to five months following hysterectomy.

A study has been made of the conditions for which conservative uterine surgery was employed in the Halstead Hospital in the past ten years and is hereby presented. There were 869 patients of all ages who had operations on the uterus producing pathologic material, benign and malignant. This group does not include cervical cauterizations, perineal repairs and uterine suspensions unless done in conjunction with uterine surgery. Of these 869 patients, 434 had conservative operations on the uterine fundus between the ages of twenty to fifty years. This includes seventeen patients who, according to operative records, had supracervical hysterectomies for myomas but follow-up records reported regular menstrual periods. In this age group ninety additional patients had supracervical hysterectomies for myomas, seventy of whom were between forty and fifty years of age. This gives a total of 524 patients with benign uterine lesions, only twenty of whom had myomas of such proportions that uterine function was not maintained until forty years of age. The follow-up record of these patients is responsible for the clinical viewpoint.

CONSERVATIVE OPERATIONS ON THE UTERUS (Halstead Hospital, October 1, 1931 to October 1, 1941)	
	Cases
Total uterine operations—all ages.....	869
Operations for benign uterine conditions.....	524
1. Defundations—20 to 50 years of age.....	434
Defundations.....	417
Supracervical hysterectomy with subsequent regular menses.....	17
2. Supracervical hysterectomy for myoma.....	90
Between 40 to 50 years of age.....	70
Under 40 years of age.....	20
Other operations for uterine conditions.....	345
The 434 defundations were performed for the following conditions:	
	Cases
1. Myomas.....	225
20 to 30 years.....	9
30 to 40 years.....	90
40 to 50 years.....	126
2. Endometrial hyperplasia or polyposis of fundal endometrium.....	185
20 to 30 years.....	14
30 to 40 years.....	93
40 to 50 years.....	78
3. Endometrial polyps.....	11
4. Endometrial sinuses.....	11
5. Degenerated polypoid endometrial tissue following x-ray therapy.....	1
6. Retained placenta.....	1
Total.....	434

In the cases of myomas, conservative operations are indicated in women before the menopause and especially if unmarried or nulliparous. Generally speaking, a woman busy with her family, if this consists of several children—not just one child—takes the menopause in her stride and it is an incident rather than an event in her life. The nulliparous woman consciously or unconsciously may be harkening to the folklore of ages past that she will no longer be attractive to her mate or that she can no longer attract a mate, following the "change of life," and a sudden menopause apparently wrecks the entire household for a while. Also the younger the woman, the more distressing and debilitating are her symptoms. When dealing with an individual case, however, it is

impossible to foretell just how a patient will react to an artificial menopause, no matter what her age or civil state or num-

no larger than a croquet ball. The pelvic bimanual examination should be confirmed under anesthesia when the pre-irradia-



FIG. 1. Myomas enucleated from a forty-year old single school teacher.

ber of children. If she is forty-five and following a myomectomy she no longer menstruates, she and her surgeon both know the tumor stimulated the uterine bleeding. If she continues to menstruate regularly until fifty years of age, she has experienced, perhaps subconsciously, a satisfactory reaction that her menstrual life terminated normally and gradually. (Fig. 1.)

In a young woman it is often possible to disturb the uterus so little that pregnancy is a possibility. This actually happened in one case. The chief value lies in the fact that it is possible to tell the patient that her entire organ was retained and child-bearing is a possibility. This softens the shock, especially to a newly married patient or one contemplating marriage, that she is permanently sterile.

Irradiation of the pelvis is commonly resorted to for bleeding myomas. The objection to this procedure is the artificial menopause it produces. Irradiation has a place in the patient at the menopause who is a bad surgical risk, e.g., the patient who has had congestive heart failure, or nephritis, or the large fat woman with a uterus

tion diagnostic curettage is done, as adnexal conditions can be missed if the obese patient guards herself during pelvic examination.

The group of patients diagnosed under hyperplasia of the endometrium or polyposis of the fundal endometrium will become smaller as our knowledge of endocrinology increases and diagnostic methods become more discerning. No uterine pathological disorder was demonstrable. The endometrium was hyperplastic such as the Swiss cheese variety which occurs with a persistent follicle cyst of the ovary, or a flat, nonovulatory type. (Figs. 2 and 3.) The bleeding was due to extra-uterine causes of several varieties.

One hundred eighty-five women had the fundus of the uterus removed to control excessive and prolonged uterine bleeding with very little to demonstrate as to the cause. Among these were patients who, e.g., lived in western Kansas or eastern Colorado who could not make a trip of three or four hundred miles more than once in a life time because of their economic status. The church or lodge may have raised the money to pay for gasoline to

make the trip. The patient lost more blood at a period than she made up in the interval and she was in a state of chronic malnutrition and nervous exhaustion. Her

she would not waken again. It was after this that her history was obtained. It is too early to give the final chapter in this case.

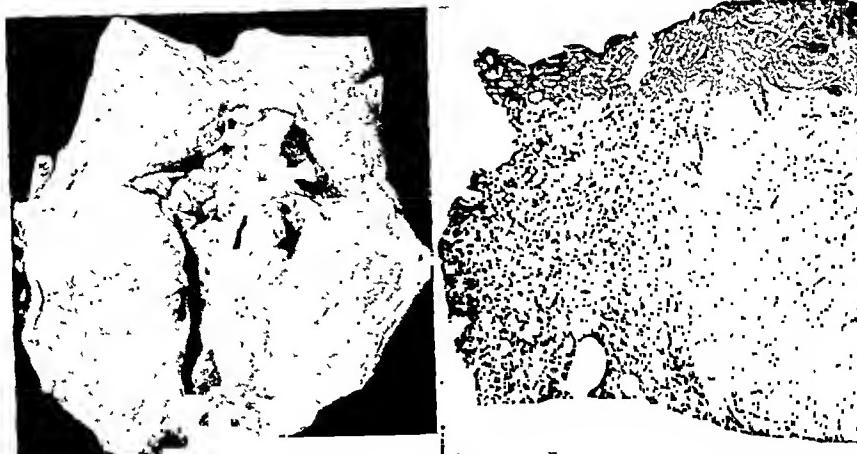


FIG. 2. Gross and microscopic appearance in hyperplasia of endometrium.

uterus may not have involuted properly, or coitus interruptus practiced over a long period produced a chronic pelvic congestion, or a deeply retroflexed uterus was tender and boggy. Removal of the uterine fundus set the patient's mind at rest. It curtailed the amount of periodic flow and the patient then had a chance to build up her nutrition and nervous state. Cervical cauterizations or repairs, perineorrhaphies and uterine suspensions or fixations were always performed in conjunction with the uterine operation when needed.

Some of these patients presented problems which might be solved if we knew enough or could control conditions as they existed. For example, a recent patient had an erotic husband who pretended his wife was a chippy and he was a travelling salesman. He insisted upon pursuing her through every room in the house and if she did not play his game, he sulked. This continued every night for eleven years. The preoperative diagnosis in this case was myoma because the uterus felt two or three times its normal size and the periods lasted nine to twelve days. During her post-operative convalescence the patient was given an amytal tablet for sleeping and the next morning she questioned the nurse as to how many of these would be required so

Endometrial polyps were the cause of menorrhagia or menorr-metrorrhagia in eleven patients. (Fig. 4.) It is possible to remove only the polyp and reconstruct the uterus. In one such case a pregnancy was later carried to term. The important point here is that if curettage does not reveal the cause of bleeding, it is good practice to look into the fundus.

Eleven cases of postoperative endometrial sinuses were cored out through the uterine fundus. (Fig. 5.) Formerly in tube resections and fundal operations the uterus was fixed to the anterior abdominal wall without peritonizing the cut surface. If a wound infection occurred, an endometrial sinus resulted in some cases. In the past seven years, the round ligaments have been used to peritonize the cut surface of the uterus and in that time only one case has had this complication. Eight patients were operated upon in the first three years of this series.

One patient had had x-ray therapy sufficient to cause partial necrosis of a polypoid endometrium. (Fig. 6A.) Another in whom curettage revealed no cause for menorrhagia and metrorrhagia over a period of four years since her youngest and fifth child was born, had a circumscribed area of retained placenta in the fundus.

(Fig. 6B.) In conjunction with this problem, Dr. W. M. Allen, of Washington University, St. Louis, recently reported in lecture

for doing a panhysterectomy: One is the possibility of a sarcoma developing in a myoma. There have been two cases of



FIG. 3. Gross and microscopic appearance of diffuse polypoid endometrium.

a case of a young unmarried woman with menorrhagia in whom history and gross findings at the curettage did not reveal the cause. While under anesthesia radium was implanted in the uterus. When the microscopic slides came through, chorionic villi were present in the curettings. In our case we dealt with a patient who gave a true history. Dr. Allen's department was dealing with a patient who thought she could put it over the doctor, so in the last analysis she is responsible for her premature castration. The point is here made again and it is the point Dr. Allen emphasized, that a definite diagnosis is the responsibility of the surgeon in charge before castration is wished upon a woman in the child-bearing years.

There are two excuses offered by surgeons



FIG. 4. Endometrial polyp with necrotic tip at x.

sarcomas in myomas in the history of Halstead Hospital and they were present as large growths when the patient presented herself for examination. Two additional cases have been set in for study. The other possibility is the development of carcinoma of the cervix left after supravaginal hysterectomy. That is possible but it is rare also. Sometimes a carcinoma already exists before the hysterectomy is done. This accounts for most cases. Examination of the cervix, and this also means the cervical canal, before myomectomy just about eliminates this excuse.

Conservative operation for bleeding is best designated defundation because only the fundus of the uterus is removed. (Figs. 7, 8, 9 and 10.) This admits of inspection of the interior of the uterus and removal of any offending area. It is always advisable to inspect the endometrium even when doing a myomectomy because an endometrial polyp and a myoma can occur in the same patient and this condition existed in one of the patients in this group. The lower half of the endometrium is usually not disturbed. Theoretically, if the collateral circulation between the ovarian-uterine ligament and cervical vessels remains intact, it permits the woman to live out her normal menstrual life; practically, patients continue to menstruate if this condition is not met.

There is the problem of recurrent operation. Among the ninety operations for supracervical hysterectomies, four were for

who found 3 per cent the record in a large group of collected cases.

Three of the cases of defundation for

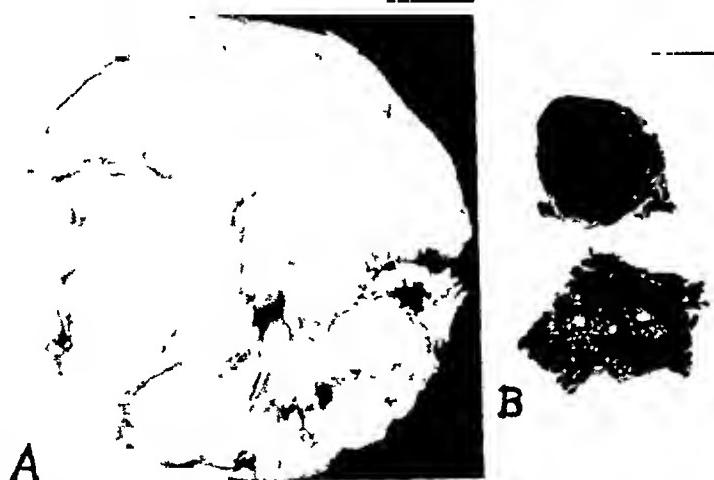


FIG. 5. A, myomectomy at twenty-eight years. B, endometrial sinus cored out through uterine fundus at thirty years. Regular and normal periods for four years since last operation.

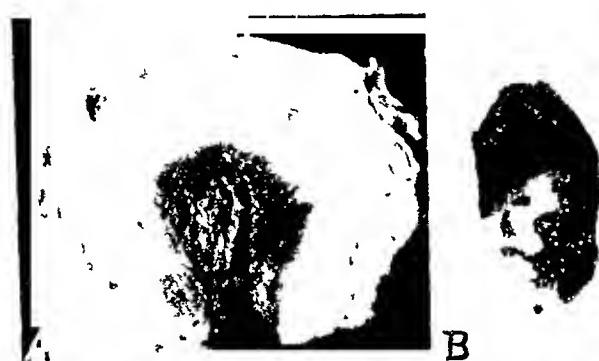


FIG. 6. A, partial necrosis of hyperplastic endometrium following insufficient dosage of x-ray therapy. B, circumscribed area of placental tissue in uterine fundus.

recurrent tumors. One of these patients had her first myomectomy at twenty-three years of age. In this series she was forty-nine years old. During the twenty-six intervening years she was a college teacher and became a professor's wife and foster mother to six children. It was worth while to her to have a balanced nervous mechanism for a quarter of a century even though she could not bear children.

The incidence of recurrence in patients up to thirty-eight years of age is 3.5 per cent. This age was selected for comparison with statistics compiled by Dr. H. E. Miller

hyperplasia of the endometrium were followed within four years by supracervical hysterectomies and three were given deep x-ray therapy.

Ten of the 524 patients died postoperatively. Two of these were among the ninety who had supracervical hysterectomies and four each had had defundations for myomas and hyperplasia of the endometrium. Four of the ten died from pulmonary infarction or embolism, two from peritonitis, two from congestive heart failure, one of these was also a diabetic and one from hemorrhage, intra-abdominal and intraperitoneal from the right uterine cornua,



FIG. 7.

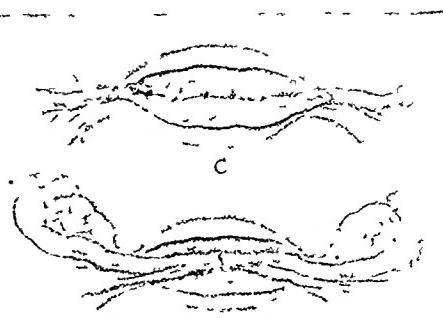


FIG. 8.

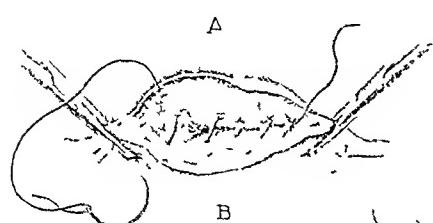


FIG. 9.

FIG. 7. A, hemostasis and incision for coning the uterine fundus. B, suture line placed deep in myometrium following conization.

FIG. 8. C, anterior and posterior uterine flaps should approximate without tension. D, cut edges of tubes and round ligaments are imbedded in musculature. E, approximation of cut edges of uterus.

FIG. 9. Round ligaments are used to peritonize the incision in the uterus.

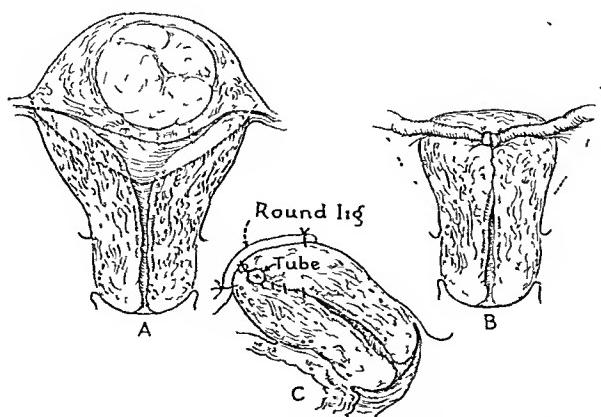


FIG. 10. A and B, comparative size of uterus following defundation for myomas. C, longitudinal section shows repair of endometrial cavity, position of tube in myometrium and peritonization of incision by round ligament.

A consideration of these facts according to percentages gives the following figures:

Patients	Deaths	Percentage
524	10	1.9
90	2	2.2
434	8	1.8
225	4	1.7
185	4	2.1

Pulmonary embolism can follow any operation and is most likely to occur in pelvic and gallbladder surgery in which large veins are abundant. We may observe the general principle never to stick through the wall of a vein nor tie about an inflamed one. But we may use every precaution and pray to the unhearing gods and still they will come when they will. In the face of postoperative streptococci infection we are almost equally helpless. The streptococcus never dies and no matter how careful the history nor how careful the preoperative examination an infection long past may be overlooked. The incidence of deaths from these causes may in the future be lessened with the use of liver extracts and sulfo compounds.

The death from hemorrhage was due to careless technic and will not occur again. The essential point in technic is that the flaps made when the diseased portion is removed must be so fashioned that they fall together without tension. If there be tension, the suture may cut through and leave a bleeding surface. If this precaution is taken and the entire suture line is completely covered with the round ligaments, a thing that can be easily done if we plan it that way, we know that union of these peritoneal covered surfaces heal within a few hours and we are secured from hemor-

rage. These operations are not done for entertainment but for a condition which menaces the life of the patient and we must accept the risk which faces us.

#### CONCLUSIONS

Conservative operation on the uterus preserves the nervous balance of the woman. In rare cases pregnancy follows but the chief value in this method of treatment lies in the fact that the woman continues to menstruate and consciously or unconsciously, she still knows she is a woman.

The operation is always possible in the hands of a surgeon who grasps the fundamental principles. Gynecologists like to think that only one trained in this specialty is capable of doing these operations. Even so, the principles of this operation as here set forth were developed by a general surgeon and have behind them an experience of thirty-five years. The operation is possible in all cases no matter what the size and number of the tumors. In large tumors a supravaginal amputation is simpler and is the operation of choice in patients in the menopause.

True, the operation carries a mortality from which we possibly can never be freed but the advantage is that the morbidity is at a minimum and herein lies the advantage of this form of treatment.

Appreciation is expressed to Dr. Arthur E. Hertzler because he made this study a possibility, to Mrs. Ruth Rose for her untiring efforts in the follow-up, and to Jim Barlow for photographs.

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# ACUTE NONSPECIFIC MESENTERIC LYMPHADENITIS

JOHN HILL TILLEY, M.D.

Attending Surgeon, Martha Gaston Hospital

LEBANON, TENNESSEE

**A**NY pathological condition, giving rise to acute abdominal symptoms and which may not require surgical treatment, is of importance from the standpoint of differential diagnosis. This is even more true should it be relatively frequent. Such a pathological condition is mesenteric lymphadenitis of the acute nonspecific variety, long recognized but not attracting much attention in the literature until recent years. Sixty-nine cases seen during a period of a little more than three years (July, 1938 to November, 1941 inclusive) indicate that it is not uncommon and that it is of importance from the standpoint of differential diagnosis. During this period, these cases have been consciously sought, the mesentery being routinely examined when no contraindication for exploration existed. This fact perhaps accounts for a greater number of cases being seen, although it has always been the rule to search for a lesion when the abdomen is opened with a probable diagnosis of appendicitis and the appendix proves to be grossly normal or exhibits a minimal pathological disorder. It is necessarily concluded that there may be an actual increase in the number of cases of nonspecific mesenteric lymphadenitis.

## ETIOLOGY

In none of the sixty-nine cases of this group was there evidence that the mesenteric lymphadenitis resulted from any of its known specific causes. No clinical evidences of tuberculosis, at original or subsequent observations, have been found except in one adult case. This patient developed evidences of pulmonary tuberculosis four months after operation. Definite association with respiratory infection has been observed and reported by some

writers. In the group of cases herein reported, the history of respiratory infection was inconstant. There were only fourteen recorded instances, with only four of the fourteen being less than ten years of age, indicating that at least in this small group of cases concomitant or recent upper respiratory infection was not an important predisposing factor. In the whole group there were only nine patients of ten years or younger showing that this disease is not one occurring only in childhood and adolescence, but very frequently in adult life. There were thirty-four patients in the age group eleven to twenty, and twenty-six more than twenty years of age, the oldest patient being forty.

The appendix has been considered a portal of entry by Brown,<sup>1</sup> Freeman<sup>2</sup> and others. There is no gainsaying the fact that removal of the appendix has been followed by cure in the great majority of cases, only two in this group having definite recurrence of pain. Wilensky<sup>3</sup> has expressed the belief that the appendix has no clinical relation to mesenteric adenitis. Careful inspection has not disclosed enlarged nodes in the average case of uncomplicated appendicitis and for obvious reasons, exploration has not been done in the complicated cases. Mead<sup>4</sup> and Wilensky and Hahn<sup>5</sup> have reported that lymphadenitis does not occur with acute appendicitis and it is particularly interesting to note that there were eleven cases of acute suppurative appendicitis in this group of sixty-nine with definitely enlarged nodes. The nodes in these eleven cases were similar in all respects to those in the other fifty-eight cases.

## PATHOLOGY

Only those cases in which the nodes have been unquestionably enlarged are included

in this study. The question as to what is a normal mesenteric node has been raised and Mead,<sup>4</sup> in an extensive investigation on the number and size of mesenteric nodes, points out that no absolutely normal mesenteric lymph-nodes are available for study except those of stillborn infants. By unquestionably enlarged nodes is meant those definitely larger than average, the average seen in laparotomy for noninflammatory lesions. In order to have a fair idea of what is average, it is necessary to make routine inspection of the mesentery. This has been done during the past several years. Those nodes classified as enlarged have uniformly been soft, pinkish in color and varying in size from  $\frac{1}{2}$  to  $1\frac{1}{2}$  cm. in their greatest diameter. While no definite ileitis has been seen, it has been noted in most instances that there was injection of the terminal ileum; specific mention of it is made in sixteen of the records. Also free peritoneal fluid in the right lower quadrant has been almost a routine finding. In those cases diagnosed as mesenteric adenitis, aside from the ones with definite and unquestioned appendicitis, the appendix has been grossly normal or at most shown injection of its serous coat. In one case there was a small Meckel's diverticulum which was not inflamed and apparently played no part in the symptomatology. A second case presented a ruptured Graafian follicle with considerable bloody fluid in the pelvis which somewhat complicated the clinical picture. Greatly enlarged nodes were numerous and the symptoms and physical signs were more in keeping with mesenteric lymphadenitis.

Complications in connection with the inflamed nodes have not been observed in this group of cases. No conglomerate masses of nodes or abscesses have been seen nor has there been any fulminating case with peritonitis such as have been reported by others. The state of the nodes at any time following operation, with removal of the appendix, is not known since the occasion has not arisen to do a second abdominal section on any patient.

#### SYMPTOMS AND PHYSICAL SIGNS

The outstanding symptoms are pain and soreness. It is with difficulty in a number of cases that an accurate description of the attack and particularly of the quality of pain is obtainable. Pain comes in attacks, some mild and others relatively severe, and the impression has been received from history taking that the pain is not infrequently aching and constant rather than colicky. In twenty-five of the sixty-nine cases, or 36 per cent, the onset of pain has been in the right lower quadrant. Tenderness has been a constant feature but has been less consistently well localized than in acute abdominal conditions such as appendicitis or diverticulitis. The impression is also gotten that the pain complained of is out of proportion to the tenderness. Tenderness along the root of the mesentery has been recorded nine times. Ochsner and Murray<sup>7</sup> have commented on the importance of this sign but it has not occurred often enough in this series to be of major diagnostic importance. An interesting feature in regard to both pain and soreness is that they have tended to vary in intensity, that is, periods of comparative ease, even with sleep alternating with bouts of pain. The only constant positive finding has been tenderness, more or less well localized in the right lower quadrant and in nine cases, along the root of the mesentery. Rebound tenderness has been found in a few cases.

The following is considered a fairly typical case history in an adult:

#### CASE REPORTS

CASE 1. Miss J. H., white, age twenty-five years, complained of deep aching immediately to the right of and below the umbilicus of twenty-four hours' duration. There was loss of appetite but no vomiting. During the past three years she has experienced a number of similar attacks, none very severe but with very definite pain and soreness lasting as a rule two or three days. Tenderness being rather sharply localized at a point approximately two inches below and two inches to the right of the umbilicus together with other signs and symptoms compatible with a diagnosis of acute appendicitis, a

laparotomy was done. The appendix showed very slight injection of its serous coat. The terminal ileum was definitely injected and its mesentery contained many enlarged nodes. Appendectomy was done and smooth convalescence followed.

The second case is cited as a rather typical instance of mesenteric lymphadenitis in a child:

CASE II. P. G., white, male of eight years became ill with epigastric and midabdominal pain, the pain recurring intermittently for twenty-four hours. He vomited soon after onset. The temperature was 102.6°F. and the leukocyte count 14,300. There was sharp tenderness together with rebound tenderness in the right lower quadrant, fairly well localized at a point approximately one and one-half inches above McBurney's point. The patient was consistent in stating that he had constant pain in the right lower quadrant despite the fact that he slept for two hours during the period of observation. While mesenteric lymphadenitis was considered in the differential diagnosis, acute appendicitis could not be ruled out and an abdominal section was done with removal of an appendix that could not possibly account for the clinical picture. The mesentery of the ileum contained many enlarged, pinkish nodes and the lower ileum was injected. Convalescence was complicated by tonsilitis.

#### DIFFERENTIAL DIAGNOSIS

The differential diagnosis of this condition is of importance and should be emphasized, inasmuch as operation may well be avoided if a correct diagnosis can be made. In this series of cases, and in most of the series that have been reported in the literature, operation has been done in a very high percentage. This is so mainly because it has not been possible definitely to rule out other acute abdominal conditions which require surgical therapy. The principal diagnostic difficulty has centered about the question of whether or not the patient had acute appendicitis. This difficulty is further appreciated when it is recalled that of this group with unquestioned lymphadenitis, eleven cases had

acute suppurative appendicitis. Foster<sup>6</sup> states that the correct preoperative diagnosis was made in only 5 per cent. In this group nine cases or 13 per cent were diagnosed lymphadenitis, and in twenty cases or 29 per cent, the diagnosis of lymphadenitis was given much consideration but the evidence was not sufficiently convincing to justify withholding operation. After having observed a considerable number of cases of lymphadenitis, certain ones have come to be suspected when the history is obtained. A child, for instance, complaining of recurring bouts of abdominal pain at short intervals together with fever, leukocytosis and tenderness which is poorly localized, should arouse the suspicion of lymphadenitis. A diagnosis would be somewhat more likely should there be a history of or the presence of respiratory infection; however, it has been an inconstant feature in the series as a whole and is certainly no regular precursor of mesenteric lymphadenitis. While not wishing to encourage procrastination in the face of a clinical syndrome indicative of acute surgical abdominal disease, it seems proper to warn that it is not to be taken for granted that a patient has acute appendicitis simply because there is a complaint of right lower quadrant pain and soreness. A diagnosis should not be arrived at without a complete history and physical examination together with, in some cases, a reasonable period of observation. The usual laboratory procedures have not been very helpful in the differentiation. From personal observation in a not inconsiderable group, there are several points in regard to the history and physical signs which dictate that the condition of mesenteric lymphadenitis be considered. Many patients have difficulty in distinguishing and describing types of pain but skillful history-taking will, in some cases, elicit the information that the pain is not colicky or gripping but that it is steady aching. In a noteworthy number, twenty-five in this series, pain began and remained in the right lower quadrant; with pain beginning

in this location, the diagnosis of appendicitis should at least be questioned. To state it another way, lymphadenitis should be considered a possible diagnosis when the onset of illness is with pain in the right lower quadrant, even if accompanied by pain in some other abdominal area.

Consideration of the location and the character of the tenderness is of paramount importance. While the tenderness is generally sharper in the right lower quadrant than elsewhere, it is not as well localized as in appendicitis. In a few cases it will be found along a line opposite the root of the mesentery. The tenderness does not grow increasingly sharper as it generally does in appendicitis; in fact, it may vary distinctly, growing less and then more severe in a few hours. The pain complained of may be quite severe but with moderate or relatively slight tenderness. Klein<sup>8</sup> has stressed the finding of shifting tenderness and the ease of diagnosis when this sign is present. It is recalled that in two adolescent patients, with atypical history of appendicitis, mesenteric lymphadenitis was strongly suspected, but appendicitis could not be ruled out. Operation was done and in both instances acute suppurative appendicitis was the lesion found. Examples such as these should cause one to pause before making an unequivocal diagnosis of mesenteric adenitis. The fear of overlooking an acute appendicitis is doubtless responsible for a large percentage of operations done. A sane attitude is that of being on the lookout for cases of lymphadenitis, knowing them to be fairly common. By keeping the condition in mind, operative treatment will be avoided in a definite number, although it seems likely that exploration will be required in the majority to establish the true pathological condition.

#### TREATMENT

Appendectomy has been the treatment in the majority of cases in this series as it has in series of cases reported by others. While appendectomy has generally been

followed by cure, it does not necessarily follow that cure would not occur without operation. Those patients who were diagnosed as cases of lymphadenitis and were not operated upon likewise recovered. Operation with removal of the appendix is indicated when acute appendicitis cannot be ruled out; with a probable diagnosis of mesenteric lymphadenitis, treatment should be conservative.

#### CONCLUSIONS

1. Mesenteric lymphadenitis is a frequent cause of attacks of abdominal pain and soreness, simulating other acute abdominal conditions of which acute appendicitis is foremost.

TABLE I  
DATA ON SIXTY-NINE CASES OF MESENTERIC LYMPHADENITIS

Average Age	Average Temperature	Digestive Disturbance	White Blood Count	Upper Respiratory Infection	No. of Cases of Acute Appendicitis
18.9 yrs.	99.6°F.	53	Av. 13,000	14	11

TABLE II  
FURTHER DATA ON SIXTY-NINE CASES OF MESENTERIC LYMPHADENITIS

Location of Pain at Onset	Location of Tenderness
Epigastrium.....	4
Midabdomen.....	25
Epigastrium and mid-abdomen.....	11
Right lower quadrant....	25
Lower abdomen.....	2
Midabdomen and right lower quadrant.....	4
	Right lower quadrant without sharp localization.....
	Along root of mesentery.....
	Vicinity of McBurney's point.....

2. Upper respiratory tract infection is an inconstant precursor or accompaniment of mesenteric lymphadenitis.

3. Mesenteric lymphadenitis has been found a number of times in the presence of acute suppurative appendicitis without a

history of abdominal pain prior to the attack of appendicitis.

4. The diagnosis of mesenteric lymphadenitis should be made more often preoperatively.

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THE excellent postoperative history of vaginal hysterectomy permits us to take the position that a patient who has borne three or four children, followed by an interval of several years' sterility, and who has a symptomatic uterus with the first degree of prolapse, is a fit subject for vaginal hysterectomy. Such treatment takes one more patient from the jaws of future uterine malignancy.

# ATYPICAL FEATURES IN THE MANIFESTATIONS OF THE ACUTELY INFLAMED, NONRUPTURED APPENDIX\*

CLARENCE E. GARDNER, JR., M.D. AND  
Associate Professor of Surgery, Duke University  
School of Medicine

CLARENCE J. SAPP, M.D.  
Intern, Starling-Loving University Hospital  
of the Ohio State University

DURHAM, NORTH CAROLINA

**A**PPENDICITIS is a treacherous disease. It is at all times totally unpredictable in regard to when, if ever, it will perforate. And while the symptoms and physical signs which it causes are often so typical that even the most inexperienced student would not fail to recognize the disease, at other times its manifestations may be so bizarre as to confuse the most clever of clinical observers.

It has been emphasized that early recognition and removal of the acutely inflamed appendix before perforation occurs represents the only means of controlling the mortality in appendicitis. To accomplish this, campaigns of education of the laity in regard to the potential dangers of abdominal pain have been undertaken by numerous agencies throughout the country. Much has been accomplished by them. However, unless the medical profession itself becomes familiar with the atypical as well as the typical features of the disease, the campaign for control of deaths from appendicitis may be only half won and the cause for failure may then properly be placed at the door of the medical profession itself.

Reid,<sup>1</sup> Boyce and McFetridge<sup>2</sup> and others have drawn attention to the frequency with which acute appendicitis manifests itself in unusual ways. They have emphasized the necessity of recognizing such cases if the appendicitis mortality is to be lowered. Nevertheless, proper recognition of this point has not been made. As a result a stereotyped picture of appendicitis remains rooted in the minds of many of our doctors. And

with it they fail entirely to make the correct diagnosis when confronted with an atypical picture of the disease.

In the typical textbook picture of appendicitis the attack begins abruptly in an otherwise healthy young adult. The first symptom is pain usually in the epigastrium which later localizes in the right lower quadrant. Pain is followed by nausea and perhaps vomiting, constipation, moderate fever, leucocytosis and localized tenderness and muscle spasm in the right lower quadrant. Such a series of events in the sequence as listed is known by even the most inexperienced of students, as well as by most intelligent laymen. Unhappily, however, the picture strictly as given is not the usual one, as a critical analysis of the first 500 cases\* of acute unruptured appendices operated upon at the Duke Hospital will show.

## AGE

Appendicitis occurs most commonly in young adults. In our experience over half of the cases occur between the ages of fifteen and twenty-five. (Fig. 1.) However, appendicitis also occurs in children and in those past the age of fifty with a frequency which makes it the commonest abdominal emergency in both of these age groups.

We have found one in every eight patients with ruptured and unruptured appendices to be either under ten or over fifty.

This relatively high incidence of the disease, the frequency with which the

\* In all cases the diagnosis of acute appendicitis was verified by microscopic study. Cases of perforated appendix are not included in this report.

\* From the Department of Surgery, Duke University School of Medicine.

diagnosis is not made until after perforation occurs, and the dangers which follow mistaken diagnoses of appendicitis when it

group such as gallbladder disease, urinary tract infection, intestinal obstruction, carcinoma of the cecum, etc.

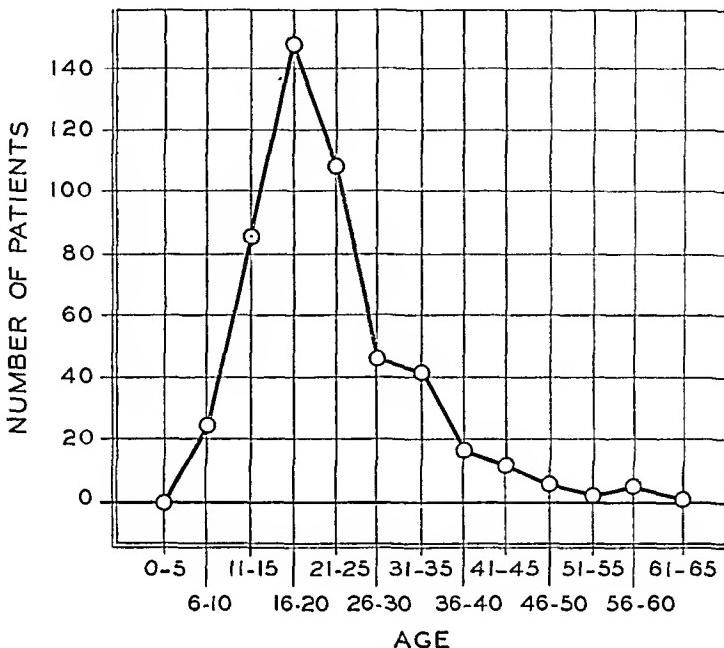


CHART 1. The age distribution of 500 cases of acute, nonruptured appendicitis.

occurs in those under ten and over fifty years of age is shown in Table 1.\*

In the group with unruptured appendices, one patient in fifteen is either under ten or over fifty. In those with ruptured appendices, however, this incidence is one patient in every four.

In the group with ruptured appendices patients under the age of ten and over fifty account for 25 per cent of the total cases. Yet in this 25 per cent of cases 48 per cent of the deaths occurred.

The tragic mistakes in diagnosing appendicitis in children or in those over fifty occur largely because the possibility of appendicitis is not even considered at these ages. In children abdominal pain and vomiting occur so frequently as a result of digestive upsets that they are likely to receive little consideration. While in those past the age of fifty the unwary doctor looks for conditions more common to this age

#### PREVIOUS STATE OF HEALTH

Appendicitis usually begins abruptly in a patient otherwise in good health. However, we have encountered acute appendicitis,

TABLE I  
FREQUENCY AND MORTALITY RATES IN PATIENTS UNDER TEN AND OVER FIFTY WITH AND WITHOUT PERFORATION

Age	Per Cent of All Nonruptured Cases	Per Cent of All Ruptured Cases	Per Cent of Those Who Died in Ruptured Group
1-10	5	15	30
50+	1.6	10	18
Total.....	6.6	25	48

confirmed by pathological examination, beginning concurrent with or during the course of chronic nephritis, acute gonorrhreal urethritis, influenza, pharyngitis, coryza, active peptic ulceration, measles, mumps, chicken pox, malaria, coronary thrombosis, chronic salpingitis, ascaris

\* Statistics on ruptured appendices are taken from a series of cases covering essentially the same period of time as the present report and published in *Surgery*, 4: 161.

infestation, pregnancy, epilepsy and pulmonary tuberculosis.

Four cases occurred in patients hospital-

had eight loose watery stools over a period of twenty-four hours before the onset of abdominal pain.

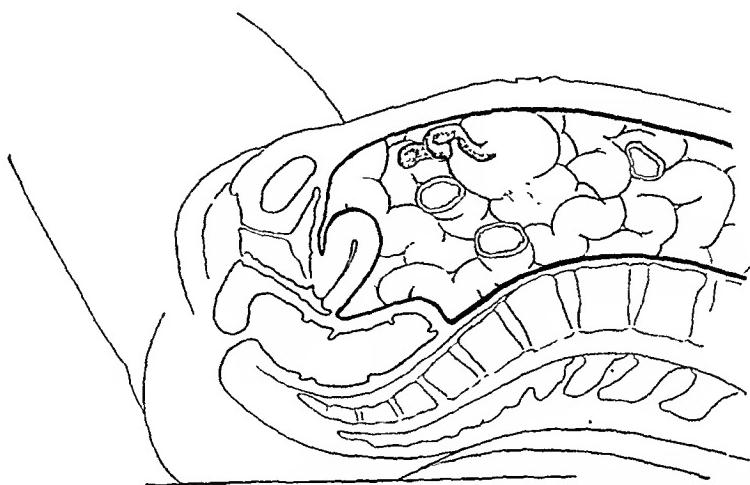


FIG. 1. The appendix occupies a position immediately under the abdominal wall. A maximum amount of local tenderness and muscle spasm is to be expected.

ized for other conditions. Two were undergoing plastic procedures, one having a tube flap raised in the right lower quadrant of the abdomen; one had osteomyelitis of the cervical spine, while another was undergoing diagnostic studies.

#### FIRST SYMPTOM

Pain is usually the first symptom in appendicitis. Murphy<sup>3</sup> has stated "the symptoms occur almost without exception in the above order (pain, nausea, vomiting, tenderness, muscle rigidity, fever, leucocytosis) and when that order varies I always question the diagnosis." Moynihan<sup>4</sup> has made the unqualified statement that if pain is not the first symptom, appendicitis need not be considered. However, pain was not the first symptom in one out of every twelve cases of our series. In them first symptoms included nausea fourteen times, anorexia eight, burning sensations in abdomen six, general malaise four, diarrhea three, vomiting three, and headache, backache and abdominal distention one each.

One patient was nauseated and vomited repeatedly for twelve hours before she had any abdominal pain whatever. Another

#### PAIN

The typical attack of appendicitis begins with abdominal pain, usually colicky in nature, which is epigastric, peri-umbilical, or generalized and then localizes in the right lower quadrant of the abdomen.

Although the majority of our patients described their pain as having been cramping, gripping or colicky, 18 per cent described their pain only as sharp, stabbing or cutting and 20 per cent only as a dull ache. In one the pain was so severe as to cause the patient to faint and it was described as excruciating or almost unbearable in five instances.

In 375 of the cases the pain began in the epigastrium, about the umbilicus or was described as generalized at onset. Seventy had pain beginning in the right lower quadrant. In twenty-nine the pain began in the lower portion of the abdomen, four in the lower left quadrant, two in the upper left quadrant, two in each flank, two in the back and one in the thorax.

In 10 per cent of the cases the pain never localized and remained generalized, peri-umbilical or epigastric until the time of operation.

All of our patients complained of abdominal pain of one type or another during their attack. Subsidence of pain, as has

#### FEVER

Moderate fever is to be expected in acute appendicitis. So unreliable, however,

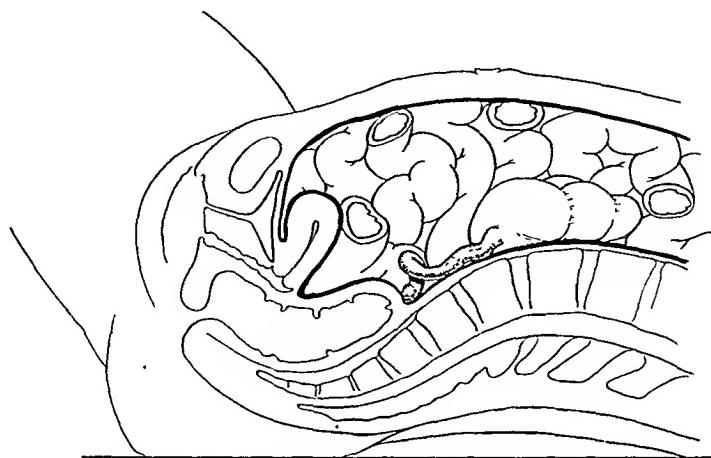


FIG. 2. The appendix lies deeply and is covered by numerous loops of bowel, mesentery of terminal ileum and omentum. Tenderness may be slight and only elicited after deep pressure. Increase in muscle tone may be entirely absent.

been emphasized many times before, may indicate gangrene or perforation of an obstructed appendix instead of subsidence of an attack.

#### NAUSEA AND VOMITING

Nausea and vomiting commonly follow shortly after the onset of pain in acute appendicitis. However, one in every six of our patients complained of neither nausea nor vomiting. Another 20 per cent complained of nausea without vomiting.

#### CONSTIPATION

It would be better if constipation be deleted entirely from the symptomatology of appendicitis for the disease should be recognized before the patient has had time to learn whether he is constipated or not. As a matter of fact, of our 500 cases only thirty-four gave a history of constipation during the attack. Thirty on the other hand complained of diarrhea. Of them, fourteen had taken cathartics which may have caused the loose bowel movements. Of the remaining sixteen patients with diarrhea, all had an acutely inflamed appendix in the pelvis.

is the mouth temperature in recording slight elevations that one can rely only on rectal temperatures. Even so, 109 or 22 per cent of our series had normal rectal temperature ( $37.4^{\circ}\text{C}$ . or  $99.2^{\circ}\text{F}$ . or below). High fevers similarly are unusual, but twenty-four of our series had rectal temperatures of  $39^{\circ}\text{C}$ . ( $102.2^{\circ}\text{F}$ .) or higher.

#### LEUCOCYTOSIS

Moderate leucocytosis usually accompanies acute appendicitis. This is known so well by the laity that we have had patients telephone and ask to come to the office not to see a doctor but for a leucocyte count only, in order that they may determine for themselves whether they have appendicitis! Yet in our experience one in every seven and one-half patients with acute appendicitis has had a leucocyte count of 10,000 or below. The usual range of leucocyte count was 12,000 to 18,000. However, seventy-nine had counts over 20,000.

#### URINE

The finding of red blood cells in the urine of a patient suffering from abdominal pain need not necessarily indicate the presence

of a urinary stone. We have found twenty-nine or one in every seventeen patients with acute appendicitis to have red blood

Rebound tenderness, either direct or referred, was present in 354 or 83 per cent of the cases in which mention was made

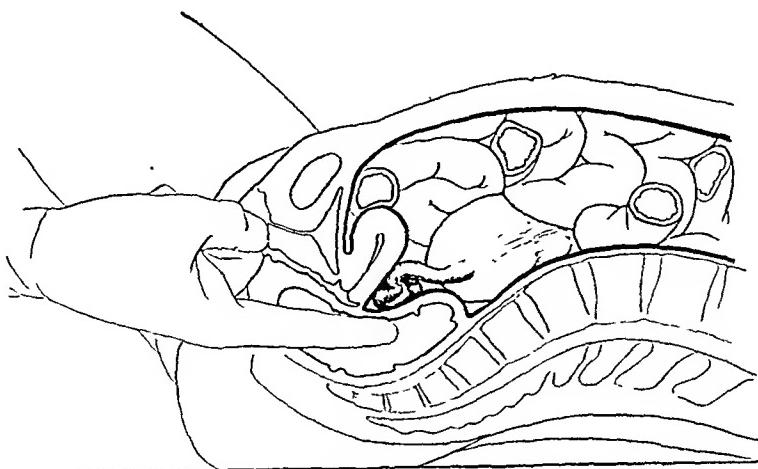


FIG. 3. The appendix lies in the pelvis where evidence of its presence may be detected only on vaginal or rectal examination. On abdominal examination signs may be vague and indefinite and found as much in the left lower quadrant as the right.

cells in the urine. This finding is probably caused by the proximity of the acutely inflamed appendix to the ureter where contiguous infection causes a mild ureteritis.

#### ABDOMINAL TENDERNESS

Abdominal tenderness of some degree has been present in all of our patients. Its degree and its location varied according to the position of the appendix and the extent of inflammation present. In 80 per cent of the cases, abdominal tenderness was confined to the right lower quadrant, though not necessarily at McBurney's point. In one out of every ten patients tenderness was present in both lower quadrants and in sixteen of these tenderness was equal in each lower quadrant. In thirty-six patients abdominal tenderness was present throughout the entire abdomen although it was most marked in the right lower quadrant. In nine cases tenderness was felt in the right flank and right lower quadrant.

Tenderness on rectal examination was present in 343 or 85 per cent of the cases in which a rectal examination was recorded. The tenderness was marked when the appendix occupied a position low in the pelvis.

of the test. The sign was elicited by causing pain over the appendix on abrupt release of pressure over the appendix or in non-involved areas of the abdomen.

#### INCREASED MUSCLE TONE

Muscle "spasm" or "rigidity" is said to be the usual finding on palpating the abdominal wall over the acutely inflamed appendix. However, in only 7 per cent of our cases was the status of the muscle tone referred to as rigidity. As a matter of fact in  $33\frac{1}{2}$  per cent of the cases there was no increase in muscle tone of any kind. In an additional 43 per cent the increase in muscle tone was recorded as slight and in only 16 per cent of the cases was it said to be marked.

#### DISCUSSION

While the variations in symptoms as seen in patients with acute appendicitis are probably caused by the fact that no two individuals ever react in the same way to the same stimulus, the variations in signs are probably anatomic and are dependent upon the degree of inflammation present and the position of the appendix.

Appendicitis may exist in all degrees of acuteness from a mild subacute inflammation to an overwhelming suppurative or gangrenous disease. However, there is no fallacy greater than attempting to predict the severity of an attack by the magnitude of symptoms or signs present. It is the variation in position, perhaps, that deceives more physicians than any other factor in the recognition of acute appendicitis. When, as in Figure 1, the appendix occupies a position immediately under the abdominal wall, it may be expected that even the lightest pressure will cause extreme discomfort and the abdominal muscles will be in a marked degree of spasm. The same appendix, however, when it is deep within the abdomen, buried under numerous loops of bowel and the mesentery of the terminal ileum and covered by the omentum may give only a minimum of signs. Tenderness in such a position may be elicited only by deep pressure, there may be no increase in muscle tone of any degree and rebound tenderness may be absent. Yet this appendix is just as acutely inflamed and just as near perforation as the one immediately under the abdominal walls whose signs were unmistakable.

On the other hand, the appendix may not be in the right lower quadrant at all. The two commonest variations of location are the lumbar and pelvic positions. In the former, signs are maximum in the flank and are most often confused with infection within the kidney. The pelvic position is the most dangerous, however, for here perforation occurs amongst loops of small

intestine into the free peritoneal cavity and a fatal peritonitis is often set up. As has been repeatedly emphasized, abdominal signs are often vague and indefinite when the acutely inflamed appendix is in the pelvis. Tenderness is not localized. It may be only slight and just as marked in the left lower quadrant as in the right. Often diarrhea is present and the unsuspecting doctor diagnoses a gastrointestinal upset or if the patient be a female, salpingitis may be suspected. Reference to Figure 3 shows why the abdominal signs in a pelvic appendix are vague. It illustrates how a rectal examination is the only means of detecting the appendix when it occupies this position.

#### SUMMARY AND CONCLUSIONS

An analysis of 500 cases of acute, non-ruptured appendicitis is presented.

At least half of the cases have been found to present unusual features of symptoms or signs in one or more instances.

Recognition of the atypical forms of appendicitis as well as the typical ones is necessary if the mortality in appendicitis is to be lowered.

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# TORSION OF THE TESTICLE

## REPORT OF CASES

MONROE WOLF, M.D.

Senior Surgeon in Urology, Charity Hospital of New Orleans; Senior Associate in Urology, Touro Infirmary  
NEW ORLEANS, LOUISIANA

TORSION of the testicle often designated as torsion of the spermatic cord is a condition resulting in a temporary or permanent partial or complete constriction of the blood supply to the testicle or to the testicle and its adnexa by a sudden vertical axial twisting of the testicular attachments (mesorchium etc.) or the spermatic cord. The fact that the occurrence of this condition is more prevalent than the earlier writers would have us expect, places an added responsibility upon the urologist and the medical profession generally, because of the necessity for a very early diagnosis and an immediate surgical interception for conservation of the testicle.

The variance in the nomenclature has caused many cases of torsion to be classified as strangulation gangrene, infarction, etc., of the testicle. This gives an added difficulty in compiling statistics from the literature, just as lack of interest of the physician in reporting his cases.

Delarsiarve is credited with reporting the first case in the year 1840. It proved to be a case of torsion of an inguinal testicle operated supposedly for a strangulated hernia.

Abeshouse, in his extensive search of the literature up to 1936, compiled 350 cases which included three personal cases. There were twenty-four cases with bilateral involvement and approximately an even division right and left where one side only was involved although several writers reported a ratio of three right side to two left side. Abeshouse also found the ratio approximately the same in cases of torsion of an undescended testicle (eleven intra-

abdominal) as compared with torsion of the completely descended testicle.

This condition can occur at any age, with cases recorded between the ages of four hours and sixty-eight years. The preponderance is before the age of twenty years during adolescence.

The author presents sixteen cases one of which was a case of bilateral cryptorchidism:

Age, Years	Color	Side		De-scended		Unde-scended	
11-20.....	White	9	Right	6	Right	3	Right
21-30.....	White	3	Right	2	Right	2	
	Colored	2	Left	3	Left	3	
31-40.....	White	1	Right	1	Right	1	
61-70.....	White	1	Left	1	Left	1	
Total.....	16		Right	9	Right	6	Right
			Left	7	Left	7	3
				16		13	

## ETIOLOGY

It is generally agreed that a normally placed and attached testicle cannot undergo torsion unless it has become detached by extreme violence, most commonly external, or surgery. Every case of torsion is attributable to: (1) a predisposing cause, always an anatomical anomaly which may be quite a number and always congenital; (2) the exciting (mechanical) factor. The actual immediate cause is due to an internal or external force which excites forceable cremaster muscular contracture. Muschat has illustrated an oblique attachment of this muscle along the cord contrary to the normal longitudinal attachment.

**I. Predisposing Causes:**

1. Undescended and imperfectly descended testicle
2. Abnormally long postmesorchium and gubernaculum
3. Absence of postmesorchium and gubernaculum
4. Very roomy tunica vaginalis
5. Complete inclosure of the lower end of the spermatic cord, testis and its appendages in the tunica vaginalis (intravaginal) (Case vi)
6. Long loose connections between the testicle and epididymis
7. Abnormal attachment of the common mesentery (mesorchium)
8. Broad and flat cord
9. Inversion, congenital nonrotation of the testical (Case i)
10. Anomalous vein to undescended inguinal testicle (Case ii)
11. Testicle and cord unattached in the scrotum postoperatively, such as in older radical repair of hydrocele testis
12. New growth of the testicle

**II. Exciting Causes:**

1. Spontaneous, no apparent cause while sleeping (Cases xii and xiii), or at rest (Cases iv, xv and xvi)
2. Muscular effort, such as straining when lifting a heavy object (Case iii)
3. Pedaling a bicycle (Case v)
4. Straining at stool (Case xi)
5. Restraining oneself while falling (Case vi)
6. Direct trauma to testicle, massaging an undescended testicle attempting to assist its descent into the scrotum (Case ii)
7. The application of a truss
8. Attempts at reducing a hernia by taxis
9. Approach of puberty, masturbation and intercourse
10. Athletic advents (Case xiv)

The recurrent type (Cases iv, xv and xvi) often gives a history of no muscular effort or strain as the exciting factor.

**SIGNS AND SYMPTOMS**

The signs and symptoms are rather characteristic but require some differentiation in a diagnostic manner from other conditions occurring in the scrotum, inguinal region or abdomen. The symptoms are associated with the circulatory disturbance created by the twist and its related local and general reactions: (1) Sudden, intense pain with increasing intensity depending upon the degree of the twist and the duration. Pain usually decreases after forty-eight hours; (2) recurrent type usually of very short duration and much less intensity; (3) displacement of the epididymis from its normal position posteriorly unless twisted 360 degrees or multiple thereof; (4) retraction of the spermatic cord and testicle; (5) swelling of the testicle and surrounding tissues; (6) light not transmitted through scrotum; (7) early increase of pain on elevation of scrotum (Prehn's sign) in torsion of descended testicle; not present in this series consistently; (8) usually negative genitourinary findings although may be associated with acute infection; (9) temperature seldom above 100°F. at onset; (10) there may be pallor and associated symptoms of mild shock; (11) there may be occasional slight nausea and vomiting early; and (12) rarely any urinary disturbance.

**DIAGNOSIS**

Consideration has to be given several confusing conditions which have to be differentiated from torsion. The undescended testicle, particularly the intra-abdominal type, creates the most confusion.

1. In the absence of the testicle from the scrotum and the inguinal canal, *torsion of an intra-abdominal testicle* should be considered, although care should be taken when there are symptoms suggesting an acute condition of the lower portion of the abdomen: (a) The appendix, having been found attached to a twisted intra-abdominal testicle, can usually be ruled out by a practically normal blood count and the

lower type temperature associated with torsion; (b) in intussusception and intestinal obstruction, the early differentiation is more difficult; (c) ureteral spasm or calculus may be eliminated by a plain x-ray of the urinary tract and intravenous urogram and an urinalysis although an occasional red blood cell may be confusing.

2. *Inguinal Testicle.* Incarcerated or strangulated hernia should be differentiated by immediate surgical intervention whether or not there is doubt. Where there is delay symptoms progressively become more exaggerated, while in torsion they become allayed. Acute adenitis is not of such a sudden onset, is associated with higher temperature and is not so common in children unless associated with cutaneous infections of the genitalia, buttock or lower extremity. The older patient will present venereal infections, simple chancroid or mixed sores. Blood count will reveal leucocytosis and increased neutrophile count. Suppuration is usually delayed.

3. *Scrotal Testicle.* Acute epididymitis may rarely be associated with torsion making the diagnosis virtually impossible, otherwise there is a history of urinary tract infection, gonorrhreal or nonspecific. The onset is more insidious with a history of pain beginning in the lumbar region and radiating to the scrotum with a decrease or complete subsidence of a urethral discharge. The swelling begins in the globus minor and is palpated posterior to the testicle. Elevation relieves pain contrary to Prehn's sign. Rectal examination may or may not reveal evidence of prostatic and seminal vesicle involvement. Acute orchitis practically always a complication of mumps is not so painful and the swelling of the testicle is greater. Acute hydrocele does not have the acute onset, is not so painful and is usually associated with infection of the epididymis or mild trauma. If the transudate is clear, it may be transilluminated. These conditions may be associated if the torsion is of several days duration. Acute hematocele is usually always accounted for by external trauma. The pain and swelling

depend upon the degree of extravasation of blood. There is usually ecchymosis of the subcutaneous tissues. The conditions may be associated as in Case vi, in which a hematoma of the epididymis could be attributed to a previous aspiration. Tumor of the testicle gives no symptoms simulating torsion unless associated with it. Cases have been recorded. A Friedman test with the urine will usually rule out teratoma.

*Pathology.* In the recurrent type of short duration with slight twist there is very slight if any damage but always a tendency to a more severe twist of a prolonged duration resulting in destruction of the testicle (Case iv). If the duration of the torsion is twenty-four hours or longer, usually edema of the subcutaneous and surrounding tissue with varying degrees of discoloration can be expected. The degree of twist controls the amount of obstruction of the blood supply to the testicle which regulates the swelling, discoloration and destruction which varies from simple complete fibrous atrophy to infarction with aseptic necrosis, effusion of blood into the testicle, epididymis and small amount of serosanguineous fluid in the tunica vaginalis or necrosis with infection resulting in suppuration and sloughing.

Microscopically, the sections show a picture of hemorrhage and necrosis. Associated new growth and tubercular epididymitis have also been recorded.

*Prognosis.* The mortality is virtually nil but the morbidity is dependent upon the time the patient is seen after onset and the delay in surgical intervention.

*Treatment.* Immediate surgical exploration should be carried out to determine the degree of disturbance of the blood supply to the testicle. If the color returns and the circulation is re-established, some form of fixation (orchidopexy) of the cord to the mesial septum posteriorly and the posterior and lateral walls of the scrotum, preferably with nonabsorbable suture material, should be done. If the color does not return to normal and the circulation appears markedly impaired, exploration of the tes-

ticle with a large aspirating needle or a small incision of the tunica albuginea for extravasated blood and possible beginning necrosis is the procedure of choice. Should extravasation of blood or necrosis be present, orchidectomy with ligation above the site of torsion is the ideal procedure.

Ormond among others advocates surgical fixation of the other testicle as a prophylactic measure.

To attempt early nonsurgical detorsion is not giving the patient the benefit of one's best judgment.

#### CASE REPORTS

**CASE I.** W., age fourteen years, complained of pain and swelling in the right inguinal region of two weeks' duration. A month or so before the present condition occurred the patient suffered much bodily trauma. He was kicked in the back pushed and thrown down upon oyster shells twice. Two weeks later his testicles ascended into the inguinal canals. He was positive they were in his scrotum before, having noticed them innumerable times. One week before admission the right one began to swell and was painful. There had been no fever, no chills, no nausea or vomiting and no urinary symptoms.

His temperature was 99° F., blood pressure, 130/70. Both testicles were in the inguinal regions. The right testicle was three times its normal size and very tender on palpation. There were no signs of inflammation, no genital sores and no urethral discharge. The scrotum was small and empty.

**Provisional Diagnosis:** Bilateral cryptorchidism with torsion of the right testicle.

Operation was performed under cyclopropane anesthesia. An incision into the right inguinal canal exposed a testicle greatly swollen and of a purple color. It was markedly adherent to the cremaster muscle and the conjoined tendon. Great care was required to preserve the continuity of the inguinal nerves in freeing it. Upon liberation of the testicle I experienced my first encounter with inversion (nonrotation) of a testicle. It was very interesting to note the lower pole of the testicle pointing upward with no epididymis attached and the attached portion of the cord and portion of the testicle from which the head of the epididymis originates below. There was considerable separation

between the testicle and its adnexa with an anticlockwise twist of the testicle of 180 degrees.

The cord was freed of its fibrous enclosure up to the internal abdominal ring. No evidence of a hernial sac was encountered. The cord was then doubled clamped, incised between the clamps and the proximal stump transfixed and ligated with No. 2 chromic catgut. The wound was then closed with the procedure commonly used in repair of hernia.

This is a case of bilateral cryptorchidism with a congenital inversion of the right testicle that underwent torsion. Earlier surgery would most probably have necessitated sacrifice of the testicle.

**CASE II.** W., age twelve years, was brought to the hospital by his mother who stated that the child had always had an undescended right testicle. The family physician had been consulted and he advised gentle downward massage of the undescended testicle three times a day. This had been done for a couple months. Two days before admission the right scrotum began to swell and became very tender. He was nauseated only once on the first day of the present illness but had no urinary symptoms and no digestive disturbances.

His blood pressure was, 110/70; temperature 99.6° F., pulse 96, respirations 24 on admission.

**Impression:** undescended testicle with traumatic orchitis.

Operation was performed under ethylene anesthesia. An incision into the inguinal canal revealed the tissues quite edematous. The hernial sac was identified and upon opening the sac an anomalous vein was found originating at the upper pole of the testicle, perforating the peritoneum through the posterior wall of the hernial sac and extending into the abdominal cavity. It was probably twisted within the abdomen as it was purple and thrombosed. No attempt was made to follow it to its termination. The vessel was 3 to 4 mm. in diameter and was lying absolutely free within the hernial sac. It was double clamped, cut and ligated near the internal abdominal ring; the proximal stump dropped into the peritoneal cavity. The peritoneum was dissected free of the cord and upon delivering the testicle into the operative field it was found to be gangrenous, the cord being twisted two and one-half times. The cord was dissected up

to internal abdominal inguinal ring, double clamped, incised, and the proximal stump transfixated and ligated with No. 2 chromic catgut. The neck of the hernial sac was transfixated and ligated with the same material and allowed to retract into the abdomen. The remainder of the wound was closed in the usual manner and a small rubber dam drain was placed in the lower angle.

This represents a case of right side cryptorchidism associated with a congenital hernia presenting an anomalous anterior, spermatic, intraperitoneal vein, instrumental in causing torsion of the testicle because of external force in the form of massage.

**CASE III.** W., age nineteen years, a plumber's helper, complained of pain and swelling of the left testicle. While lifting a bath tub in the morning the patient experienced sharp, acute pain in the left scrotum radiating from the lower portion of the abdomen. The pain was momentary, but a general feeling of dull discomfort was noted during the day. At night he noticed the left testicle began to swell, became tender and he again developed acute scrotal pain, so he entered the hospital for relief.

There was no urinary disturbance. There was a small penile sore of two months' duration and he gave a history of one year's antileptic therapy. His blood pressure was 116/80; temperature 98°F., pulse 100; respirations 24.

The left testicle and epididymis were enlarged, indurated, and tender and the cord was freely movable. Some relief of pain was secured by elevation of scrotum. There was a superficial irregular ulceration of the glans penis. The prostate was negative for any pathological condition per rectum.

Tentative diagnosis: Torsion of cord.

The blood Wassermann test was negative. The maximum temperature was 98°F. He was discharged the day following admission with a diagnosis of acute epididymitis.

One week later the patient was readmitted complaining of severe pain and swelling of the left testicle.

The intern's note stated: "Testicle has not subsided." Diagnosis: acute orchitis. The pre-operative diagnosis was probable torsion of the left testicle.

Spinal anesthesia was given and an incision 3 inches long was made in the anterior scrotal wall exposing the spermatic cord and testicle. The testicle was markedly enlarged and of a purple color. The epididymis appeared on the anterior mesial aspect due to 180 degrees torsion of the cord about  $\frac{1}{2}$  inch above the pole of the testis.

The testicle was markedly engorged with thrombotic exudate; the epididymis was markedly engorged with the same material. The cord was double clamped and incised, the proximal stump transfixated and ligated with No. 2 chromic catgut. The scrotal cavity was drained with a small piece of rubber dam. The skin was closed with a continuous suture of No. 0 plain catgut.

This is a case of torsion in which there was a disagreement in diagnosis on primary admission. It is probable that the testicle could have been saved had there been an exploration although he was admitted about ten hours after onset of symptoms.

**CASE IV.** W., age fifteen years, a schoolboy, was referred to my office by the family doctor because of painful, swollen testicle of twelve days' duration, after there had been no relief of swelling, following rest in bed with elevation of scrotum and the application of an ice bag. There had been no fever.

On arising from his seat in a picture show, the patient experienced slight, sudden pain in his right testicle which persisted. Swelling of the testicle with added pain awakened him during the night. Upon calling his family doctor, he was advised to remain in bed and elevate the scrotum applying an ice bag. The patient gave a history of previous attacks of slight, sudden pain of very short duration without swelling of the testicle.

His blood pressure was 120/60; temperature 98.6°F.; pulse 84. The right testicle was markedly swollen and tender; pain radiated up along the cord into the inguinal region on elevation. The patient was referred to Charity Hospital for surgery with a tentative diagnosis of torsion of the testicle.

Operation was performed under ethylene gas anesthesia. An incision through the anterior surface of the scrotum exposed the cord which was freed from the surrounding adhesions and elevated by an encircling piece of tape. The cord and testicle were markedly adherent to

the scrotum necessitating blunt dissection to free them. The testicle was found to have a dark red hemorrhagic color, but there was no evidence of torsion. The torsion had evidently become untwisted and corrected itself as on previous occasions, but too late to avoid irreparable damage.

The cord was double clamped and incised, the proximal stump transfixated and ligated with No. 2 chromic catgut. A small twisted silk-worm gut drain was placed through a stab wound. The skin was closed.

This represents a case of recurrent torsion of the testicle in which the detorsion was too late to prevent marked damage during the last attack. It is possible fibrosis and atrophy would have resulted with more delay and rest.

CASE V. W., age sixteen years, a delivery boy, was seen by me at the request of the admitting officer and diagnosis of torsion was made. The patient was admitted to the observation ward and operated upon by the senior resident three hours later.

Four days before admission the patient stated that he accidentally struck his right testicle while riding his bicycle and suffered slight pain for a very short while. The day before admission the pain recurred and radiated up toward his inguinal and lumbar regions. Application of medication and warm compresses gave very little relief and the testicle began to swell so he came to the hospital.

His blood pressure was 120/80; temperature 99°F., pulse 92, respirations 20. The scrotum was enlarged and reddened; the right testis appeared enlarged and tender.

Operation was performed under spinal anesthesia. An incision of the scrotal wall was made to the tunica vaginalis which was slightly distended with bloody fluid. Upon opening it the testicle and epididymis were found to be gangrenous. The testicle was twisted one complete turn just above the epididymal tail. The vas and cord were clamped and incised and ligated separately above the twist with No. 2 chromic catgut. The scrotum was closed with a continuous lock switch No. 1 chromic catgut.

This is a case in which neglect on the part of the patient necessitated sacrificing a testicle.

CASE VI. C., age twenty-seven years was seen by the author after the patient had been under observation by a compensation insurance surgeon for a period of two weeks because of a slightly painful, markedly swollen right testicle. The attending physician stated that a small amount of bloody fluid had been aspirated from the mass shortly before I was asked to see the patient.

The onset of pain and swelling of the testicle followed about two hours after restraining himself from falling while pushing a hand truck on the wharf. There was a history of no previous similar attack and no recent venereal disease.

There was no evidence of a venereal disease. The right scrotum contained a slightly tender mass about the size of a golf ball which was adherent to the skin; temperature was 98°F. This was considered a case of torsion, but because of the lack of more severe pain at the onset a Friedman test was recommended and performed with a negative report.

One week later the author was requested to assist at a surgical exploration of this case. Under ether anesthesia an incision was made through the skin and thickened subcutaneous tissue and tunica vaginalis which was adherent to the epididymis twisted anteriorly 180 degrees. Upon freeing the adhesions a hematoma was liberated from the epididymis and the twisted testicle and cord resumed their normal position, the testicle regaining its normal color. The testicle was anchored to the septum and posterolateral walls of the scrotum after which the scrotum was sutured.

The above is a case of 180 degrees torsion of an intravaginal testicle of three weeks' duration in which the circulation appeared to be unimpaired.

CASE VII. W. M., twenty-eight years old, complained of swelling of the left testicle. He first noticed swelling and pain in the left scrotum with blueness two days after he was hit in the region of his scrotum by a large soft indoor base-ball. There was marked ecchymosis of the scrotum with swelling of the left testis which appeared to hang at right angles to the cord. Pain increased on elevation (Prehn's sign), and the patient was referred to Charity Hospital.

Pontocaine (5 mg. in 3 cc. of glucose solution 10 per cent) failed as a spinal anesthetic after waiting twenty minutes, necessitating

ethylene anesthesia. An incision over the left scrotum exposed the testicle and cord. The testis was found practically normal, although the veins in the cord were markedly enlarged and partially thrombosed, with a markedly elongated mesorchium, the testis lying at right angles to the cord. Another incision was then made over the left external abdominal inguinal ring exposing the spermatic cord which was elevated in the wound and the anterior group of veins were separated for about 2 inches, double clamped and ligated and the intervening section excised. The proximal stump was anchored by means of its ligature through the fascia of the external oblique muscle.

The testicle was then fixed to the scrotal septum with two mattress sutures of No. 2 Deknatel silk. Both wounds were then closed with plain No. 0 catgut.

This is a case of torsion of the testis with an associated elongated mesorchium and varicocele.

**CASE VIII.** W., nineteen years of age was first admitted with the following diagnosis: (1) Bilateral indirect inguinal hernia; (2) undescended right testicle; (3) hypospadias; (4) atrophic left testicle. He was referred to the clinic for treatment with Antuitrin S. He was re-admitted three months later with pain in the right testicle of ten hours' duration. When voiding urine the patient was stricken with a severe, cramping pain simulating pressure on the right testicle in the right groin.

The patient had had numerous previous attacks of pain of a similar character of the undescended right testicle, which he had been able to relieve by downward pressure with his fingers. He had not been able to relieve this attack of pain. Coughing greatly increased the pain and there had been no desire to void since the onset.

There was a small firm, tender, fixed mass about the size of an English walnut in the right inguinal region; temperature was 98.6°F., pulse 68, respirations 22.

Operation was performed two hours following admission. Pontocaine (10 mg. in 3 cc. of glucose solution 10 per cent) as a spinal anesthetic was ineffective after waiting twenty-five minutes, therefore, cyclopropane was supplemented.

An incision was made down to the base of the scrotum exposing the inguinal canal; a cherry-

red mass was visualized. The testicle appeared to be normal in size and color; it was attached only to the epididymis at the globus major. The epididymis and vas being pendulous became twisted creating the mass.

The hernial sac was dissected free of the vas and vessels, ligated at its neck and excised. The cord was freed of all fascial attachments and found elongated sufficiently to allow placement of the testicle into the newly made scrotal cavity where it was retained by placing a mattress suture of No. 2 Deknatel silk from both lower posterolateral surfaces of the testicle through the bottom of the scrotum, tying them separately over gauze sponges. The hernia was repaired in the usual manner.

At 4 A.M. of the second postoperative day there was a sudden onset of coughing with left chest pain; temperature 103°F., pulse 116, respiration 36. Change of position with inhalation of oxygen and forced coughing caused expulsion of a mucous plug relieving atelectasis. At 6 A.M., temperature was 100.6°F., pulse 80, respirations 32; noon temperature was 98.6°F., pulse, 80, respirations 28.

Recovery was uneventful following the above incident.

This is a case report of a youth with several congenital urogenital deformities, giving a history of apparent recurrent torsion of an epididymis and proximal vas deferens (right). Postoperative atelectasis developed with early spontaneous expulsion of a mucous plug which otherwise should necessitate immediate bronchoscopy. There was an atrophied left testicle probably due to torsion associated with a congenital hernia.

**CASE IX.** W., age twenty-six years, a medical student, experienced pain in the right testicle. He stated that he was awakened early in the morning with dull aching pain in his right testicle. There was no associated nausea, vomiting, chills or fever, but the patient stated that pain radiated up into his right groin and right lower quadrant. Pain was continuous and persisted to the time of examination. Some swelling and marked tenderness of the right testicle developed. There had been two previous similar attacks, one at sixteen years of age, and another four months previously to this attack in question. Both attacks also came

on while at rest and subsided without complications in six to eight hours.

The right testicle was enlarged to twice its normal size with marked tenderness which increased on elevation of the testis (Prehn's sign); temperature was 98.6°F., pulse 80, respirations 20, blood pressure 120/80.

Operation was performed one hour after examination and diagnosis. Novocaine (½ per cent) infiltration was used to block the cord and inguinal canal. An incision through the serosal tissues exposed a cherry red mass which proved to be the testis. Upon bringing this mass into the wound, the testicle was found to be rotated clockwise 180 degrees. Upon un-twisting the rotated testicle it regained normal color immediately. There were two distinct glistening cystic areas in the globus major of the epididymis. These cysts were punctured with a sharp pointed scalpel. The testis was then anchored to the scrotal septum with three mattress sutures of No. 2 Deknatel silk, after which the scrotum was closed with a continuous plain No. 0 catgut suture.

There has been no further discomfort. The testicle is fixed in the scrotum with some infiltration at the site of the fixation sutures. The cysts have since refilled; aspiration revealed spermatozoa.

The preceding is a case of recurrent torsion of the testis operated upon one and one-half hours after examination. Multiple cysts of the epididymis were found and a perfect recovery followed.

#### FIVE CASES COLLECTED FROM THE RECORDS OF OTHER SERVICES AT CHARITY HOSPITAL

**CASE X.** W., age fifteen years, a schoolboy, complained of pain and swelling in the left testicle. Two days before while sitting quietly in bed he was seized with a sudden, violent pain in the left testicle. The left side of the scrotum rapidly enlarged and the pain became more severe. Ice bag and support brought very little relief. He had no fever. The patient had had several attacks of a similar nature during the past five years, of less intensity and of short duration. The serotum had a bluish discoloration. The left epididymis and testicle were swollen and tender. Temperature was 98.6°F.

Operation was performed under spinal anesthesia (tutocain 100 mg.). A low posterior incision was made in the serotum liberating the

testicle and epididymis with the tunica vaginalis. The entire mass was of a bluish black color. On opening the tunica a small amount of dark clotted blood was liberated. The testicle, epididymes and 1 cm. of the cord were dark and hemorrhagic. About 1 em. above the testicle the cord was found to make a complete twist causing complete strangulation of the blood supply. Excision was done above this point and the vas and vessels were ligated separately. A small rubber drain was left in the serotum.

This was a case of recurrent partial torsion which developed a permanent torsion of 360 degrees resulting in gangrene.

**CASE XI.** W., age thirty-seven years, a chauffeur, complained of pain in the right lower quadrant radiating to the right testicle. He was admitted with a diagnosis of possible ureteral calculus and was x-rayed on the way to the ward.

Two months previous the patient had a sudden attack of severe, cramp-like pain in the right lower quadrant, radiating to the right testicle. This pain lasted about one and one-half hours. The condition did not recur until about 7:30 A.M. on the day of admission with more severe pain and of longer duration. There was slight nausea, no vomiting and no temperature; his bowels had been regular. Blood pressure was 130/90; temperature 99.4°F., pulse 74, respirations 22. The patient was discharged with a diagnosis of possible torsion of spermatic cord.

There is the possibility of recurrent torsion in this case.

**CASE XII.** W., age fourteen years, a schoolboy, complained of pain in the right testicle. A few hours before while in a squatting position watching the shoeing of a horse, he attempted to rise and when doing so developed a severe pain in his right testicle which became exaggerated on standing or walking. He immediately came to the hospital for treatment. His blood pressure was 110/65; temperature 99.2°F., pulse 90, respirations 18.

There were pain and tenderness in the right lower quadrant above Poupart's ligament when traction was made on the right testicle; there was no rigidity. The right testicle was drawn upward in the serotum and was extremely painful on downward traction. There

were no color changes. Diagnosis: Torsion of the right spermatic cord. The condition corrected itself the day following admission.

This is a case of torsion of the right testicle in which spontaneous detorsion resulted. There has been no follow-up.

**CASE XIII.** C., age twenty-five, a farmer, complained of a swollen left testicle. The patient stated that he had "clap" for the past four to five weeks. He had had several previous attacks which were apparently cured. Swelling of the left testicle began one week ago accompanied by intense pain and abdominal cramp. He had been having some difficulty urinating lately. The pain in the testicle had frequent exacerbations and the swelling had been gradually increasing. His temperature was 99°F., there was slight rigidity and some tenderness in the lower left quadrant.

There was a creamy white urethral discharge. The left testicle was markedly swollen and hard. The testicle and spermatic cord were very tender. Rest in bed, elevation of the scrotum, and ice bag were ordered for one week. The testicle grew larger and larger and there was an irregular temperature.

Operation was performed under spinal anesthesia (tutocain 100 mg.). An incision into the side of the scrotum exposed the testicle and its appendages revealed no suppuration. The testicle and epididymis were found to be gangrenous because of a twist found in the cord just above the superior pole of the testicle. There was evidence of a chronic inflammatory process with many adhesions.

The cord was doubled clamped, incised, transfixated and tied with No. 2 chromic catgut. The scrotum was closed with interrupted sutures.

This is a case of torsion of the testicle associated with a subacute urethritis most probable gonorrhreal, although there is no record of smear.

**CASE XIV.** W., age sixty-eight years, a farm hand, complained of swelling of the left half of the scrotum. He stated that four days previous he suffered with diarrhea and while straining at stool he had a sudden severe, sharp, knife-like pain in the left inguinal region. Immediately the left half of his scrotum began to swell and become blue. It continued to swell

and be painful and the color became almost black. His doctor advised an ice bag to his scrotum. There was no relief of the pain and swelling, so he decided to come to the hospital.

His temperature was 99°F., pulse 86, respirations 24, blood pressure 98/60. The left testicle was swollen and fairly soft; the scrotum was edematous. The prostate was slightly enlarged. The patient was discharged after ten days and his condition was improved. Diagnosis: Torsion of the cord; prostatic hypertrophy.

This is a possible case of torsion undergoing resolution after fifteen days, probably resulting in fibrosis and atrophy.

#### TWO CASES FROM THE RECORDS OF TOURO INFIRMARY

**CASE XV.** W., age fifteen years, a schoolboy, was admitted to emergency clinic (General Surgery) complaining of pain in the left testicle of two hours' duration. The pain was of sudden onset while lying on a bed one-half hour after chopping wood. There was no history of trauma.

Examination revealed a tender and firm left testicle of normal size; the epididymis was firm and tender; blood pressure was 142/80, temperature 99.4°F. The patient was sent to the operating room but the operation was postponed.

The urological consultant diagnosed induration of the left testicle and suggested hot water and expectant treatment. The patient was seen by the author six months later with marked atrophy of the left testicle. It was about one-fourth size of the right testicle. The right testicle was freely movable in the scrotum with a wide separation of the testicle and the epididymis.

This is a case of torsion appearing for treatment soon after an acute onset. Severe atrophy would probably have been avoided had the original plan of surgical intervention been followed.

**CASE XVI.** W., twenty-three years of age, a college student, complained of intermittent severe pain and then constant dull pain in the left testicle from early in the morning. There was no history of trauma or venereal diseases. Pain was not accentuated by palpation and

there were no abnormalities detected. Temperature was 98.6° F. He was discharged after two days with a diagnosis of torsion of the spermatic cord.

Evidently, this is a case of partial torsion which had corrected itself. There has been no follow-up.

#### SUMMARY

1. A definition of the condition is given as interpreted by the author.

2. The incidence of side involved in the author's cases of descended testicles coincides with the statistics compiled by Abeshouse on 350 cases. Contrary to his records in cases of completely descended testicles as compared with undescended testicles, the author's series present thirteen to three in sixteen cases.

3. The author has added another cause to the numerous predisposing congenital anatomical defects resulting in excessive abnormal mobility of the testis and spermatic cord. A case is presented of undescended testicle with a congenital hernia in which there was an anomalous intraperitoneal anterior spermatic vein. Some exciting causes are tabulated.

4. The signs and symptoms are tabulated with stress being placed on the sudden onset with severe pain in the testicle and cord usually with retraction and elevation of the cord and testicle, a very slight rise in temperature, the early presence of Prehn's sign and the abnormal position of the epididymis unless there is a rotation of 360 degrees.

5. Diagnosis is to be differentiated from appendicitis, intestinal obstruction, ureteral spasm or calculus, incarcerated inguinal hernia, inguinal adenitis, epididymitis,

orchitis, acute hydrocele and hematocele and tumors of the testicle.

6. The pathological condition is considered, varying from no damage to complete destruction with atrophy and complete disappearance of the testicle.

7. Prognosis depends upon early interception.

8. Treatment is described insisting upon immediate surgical intervention.

#### CONCLUSIONS

1. There is no place for conservative treatment in torsion of the testicle even though the diagnosis is doubtful.

2. Whenever the symptoms are suggestive and the diagnosis is doubtful, an immediate surgical exploration of the testicle is indicated. If the testicle is not normally fixed in the scrotum, an attempt should be made to fix it if there is no evidence of irreparable damage.

3. The author's technic for radical surgical repair of hydrocele testis is recommended for hydrocele repair to prevent postoperative torsion of the testicle.

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# ULTRAVIOLET BLOOD IRRADIATION THERAPY (KNOTT TECHNIC) IN ACUTE PYOGENIC INFECTIONS\*

GEORGE MILEY, M.D.

Clinical Professor of Pharmacology, Hahnemann Medical College

PHILADELPHIA, PENNSYLVANIA

DURING the past three years we have used ultraviolet blood irradiation therapy in 151 unselected serial cases of acute pyogenic infection as a method of controlling infection. The Knott technic which was employed in all cases consists of withdrawing and citrating a carefully predetermined amount of a patient's blood and immediately passing it through a hemo-irradiator, a machine that properly irradiates the citrated blood and returns it intravenously to the patient. The hemo-irradiator is by design so constructed as to regulate all dosage factors and, by the precision of its operation, makes the administration of this therapy a safe and efficient procedure. In this paper we shall briefly review a few known biochemical and physiological effects of ultraviolet energy, give the essential details of the Knott technic, and present the results obtained by us in controlling acute pyogenic infection. A correlation of the observed clinical effects of this therapy with several established biochemical and physiological effects of ultraviolet will be made wherever this is possible.

Since 1877, when Downes and Blount first described a marked bactericidal effect of ultraviolet light, many biochemical and physiological effects of ultraviolet have been discovered and utilized. The high bactericidal properties of ultraviolet have been conclusively demonstrated due to the excellent early work of Downes and Blount,<sup>1</sup> Ward,<sup>2</sup> and more recently, of Coblenz,<sup>3</sup> Bayne-Jones,<sup>4</sup> Wyckoff,<sup>5</sup> Bachem and Dushkin,<sup>6</sup> and others.

According to reports of Jodlbauer and von Tappeiner,<sup>7</sup> and Noguchi,<sup>8</sup> and later,

to the original studies made by Macht,<sup>9</sup> Schubert,<sup>10</sup> and Welch,<sup>11</sup> it becomes clearly evident that ultraviolet has a very powerful detoxification effect. The rapid and complete inactivation of snake venoms and bacterial toxins are excellent examples of what may be accomplished by ultraviolet.

The production of peripheral vasodilation following external application of ultraviolet in animals and humans has been shown by Balderrey and Barkus,<sup>12</sup> T. Lewis,<sup>13</sup> Krogh,<sup>14</sup> Ellinger<sup>15</sup> and Kawaguchi.<sup>16</sup>

The ability of blood irradiated with ultraviolet to absorb oxygen more readily than nonirradiated blood has been demonstrated by Mayerson and Laurens,<sup>17</sup> Miley<sup>18</sup> and Harris.<sup>19</sup>

The presence of secondary emanations in blood following its exposure to primary emanations of ultraviolet has been detected and reported by Wels,<sup>20</sup> Becker and Szendro<sup>21</sup> and Rahn.<sup>22</sup>

In 1897, Raab<sup>23</sup> first noticed and described the lethal action of acridine on paramecia exposed to light contrasted with its nonlethal action in the absence of light. This phenomenon was called photodynamic action or photosensitization. Jodlbauer and von Tappeiner<sup>24</sup> soon afterward followed up this discovery with a series of brilliant experiments showing that sensitization of a biological system to visible and ultraviolet light can be produced by various fluorescent dyes. In our work today we are most concerned with the fact that sulfa drugs produce photosensitization and photoallergic effects in man. This latter principle has been described by Epstein<sup>25</sup> and Blum.<sup>26</sup> We have reported<sup>27</sup> recently the presence of untoward photosensitive

\* From The Hahnemann Medical College and Hospital of Philadelphia.

effects such as convulsive seizures, renal shut-down and a rapid increase in toxic symptoms when sulfanilamide, sulfathia-

theless, subject to many disadvantages contingent upon any attempt to obtain general or systemic effects by the external

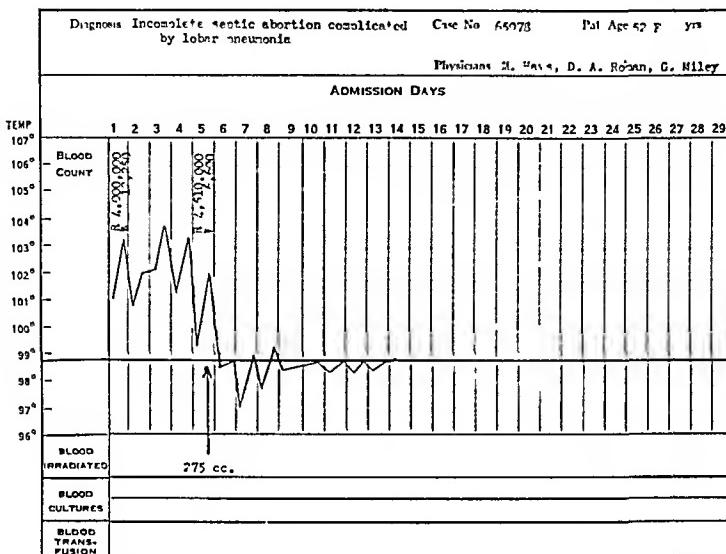


FIG. 1. In this patient lobar pneumonia developed during intensive sulfathiazole therapy given to control sepsis secondary to incomplete septic abortion. Consequently the patient's condition became extremely precarious. Within twenty-four hours following blood irradiation, a marked detoxification effect, coincident with the temperature drop shown, was observed to occur. The patient convalesced uneventfully during the ten remaining hospital days.

zole or sulfapyridine were given within the first four or five days following ultraviolet blood irradiation therapy and the complete absence of such effects when ultraviolet blood irradiation therapy was given as soon as an hour after blood levels of these drugs had been ascertained to be at a maximum.

Finally, the effect on general resistance has been the subject of extensive work and has been reviewed carefully by Clark.<sup>28</sup> It is common knowledge that certain, as a rule, minimal erythema doses of externally applied ultraviolet radiations stimulate the general resistance of animals and human beings to infection.

In addition to these references, work in this field has been well described by Blum,<sup>29</sup> Duggar,<sup>30</sup> and Ellis, Wells and Heyroth.<sup>31</sup>

In attempting to use these known effects therapeutically, it had been found necessary to depend on external application. Valuable though such a method may be when local effects are desired, it is, never-

use of therapeutic agents. It is apparent, then, that if ultraviolet energy could be administered directly to the blood stream (i.e., intravenously) safely and efficiently in easily controlled dosage, one might expect the elimination of certain disadvantages of external application, such as irregular absorption in rate and amount of energy with inconstant, negative or overdosage effects. Furthermore, in such event one might hope for the constant and safe production of certain of the beneficial physiological effects already mentioned, e.g., the bactericidal effect, a detoxification effect, a rise in general resistance.

#### TECHNIC AND DOSAGE

In 1934, Knott and Hancock<sup>32</sup> reported the rather spectacular recovery of two apparently moribund cases—one of septicemia, one of brain abscess—following the ultraviolet irradiation of a predetermined amount of the individual's blood and immediate reinjection of that blood. The

technic of this method of irradiating blood has since been somewhat modified by Knott and in its modified form is that

between the irradiation chamber and the mercury burner.

The water-cooled type of mercury-

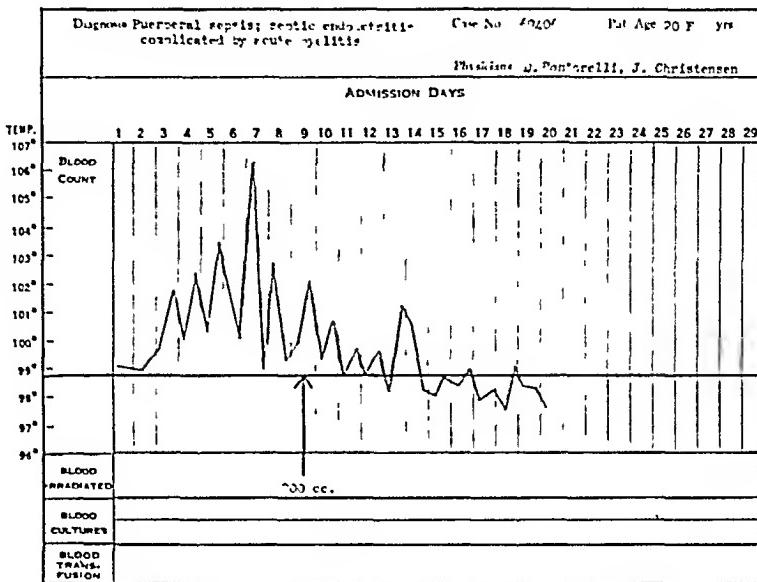


FIG. 2. Ultraviolet blood irradiation therapy was administered to this young woman suffering from postpartum septic endometritis and acute pyelitis when toxic symptoms began to increase rapidly over a period of forty-eight hours starting on the fifth postpartum day. Within twenty-four hours following blood irradiation a complete detoxification effect was observed and an uneventful eleven-day convalescence ensued.

referred to in this paper as the Knott technic of ultraviolet blood irradiation therapy.

The irradiation of blood with ultraviolet energy with a hemo-irradiator (Fig. 7) is made possible by a combination of three devices: (1) a modified Knott irradiation chamber, (2) an automatic transfusion pump, and (3) a water-cooled, mercury-quartz burner.

The irradiation chamber is a silver, disk-shaped, quartz-windowed container through which the blood passes and in which it is irradiated.

The automatic transfusion pump allows blood to be pumped by propulsion through rubber tubing and through the Knott chamber at whatever rate is desired, thus carefully controlling the time of exposure to ultraviolet energy of each cubic centimeter of blood as it passes through the chamber. An intermittent exposure is obtained by a rotating shutter interposed

quartz burner is used and is fastened approximately 1 cm. from the quartz window of the irradiation chamber through which the blood is pumped. The ultraviolet rays are confined to a closed, highly polished steel housing and have the same intensity as if at actual contact.

The clinical application of this combination consists of withdrawing a pre-determined amount of venous blood from an individual, citrating it (one part 2.5 per cent sodium citrate to five parts blood) and immediately returning it to the same individual through the hemo-irradiator to the vein from which it was withdrawn. The immediate return to the venous circulation of irradiated blood through a closed system obviates the rapid loss from irradiated blood of ultraviolet energy, which occurs if blood is, for example, spread out in open flat receptacles during irradiation.

In using this method it is necessary to be sure that three important factors are kept

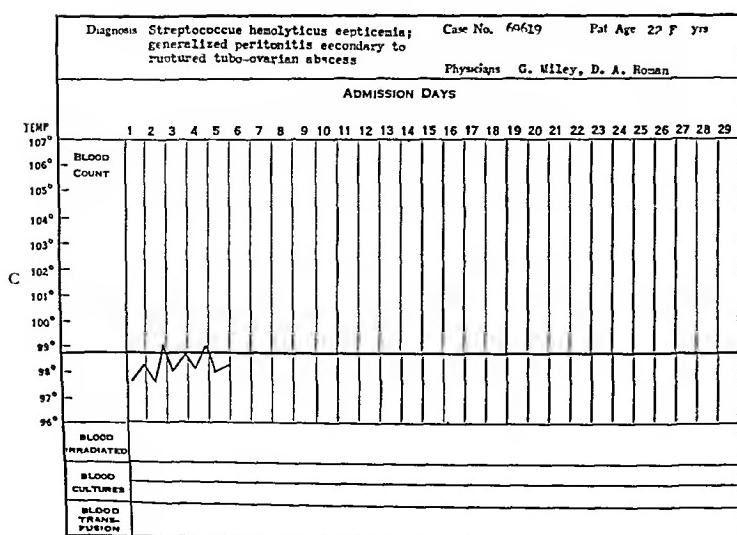
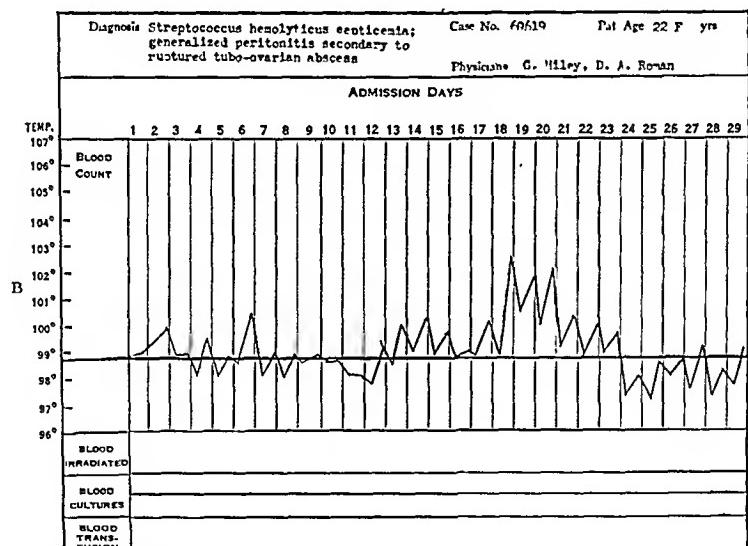
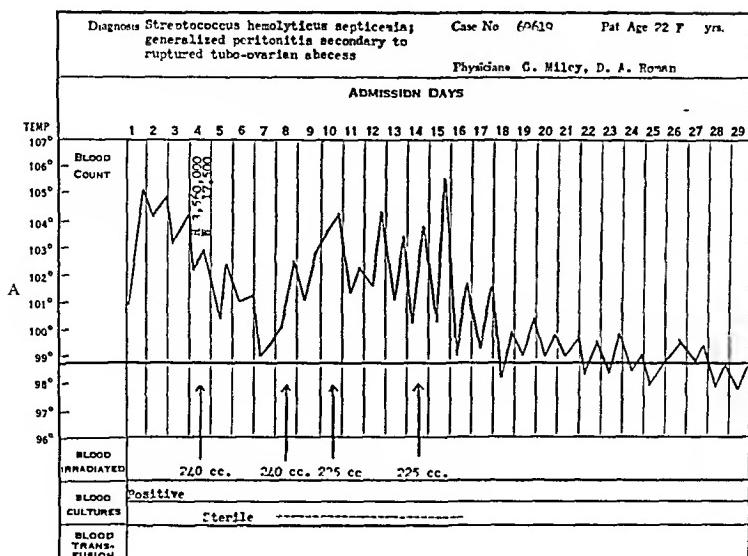
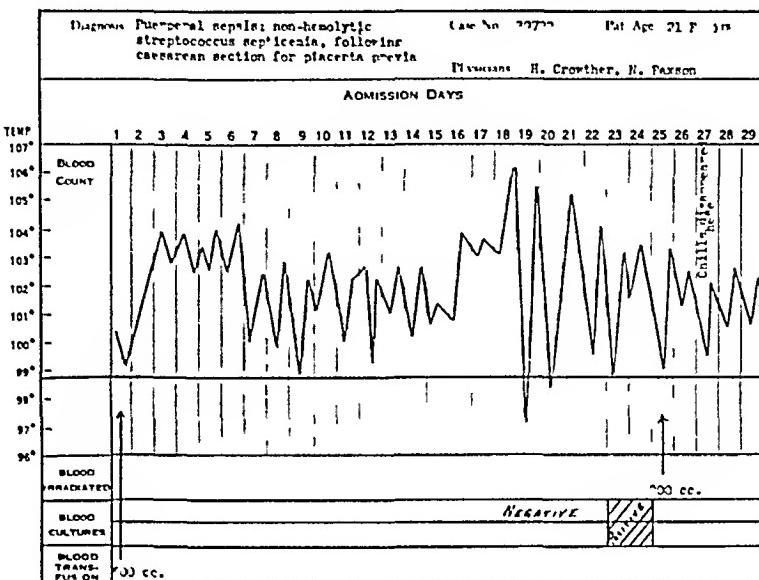


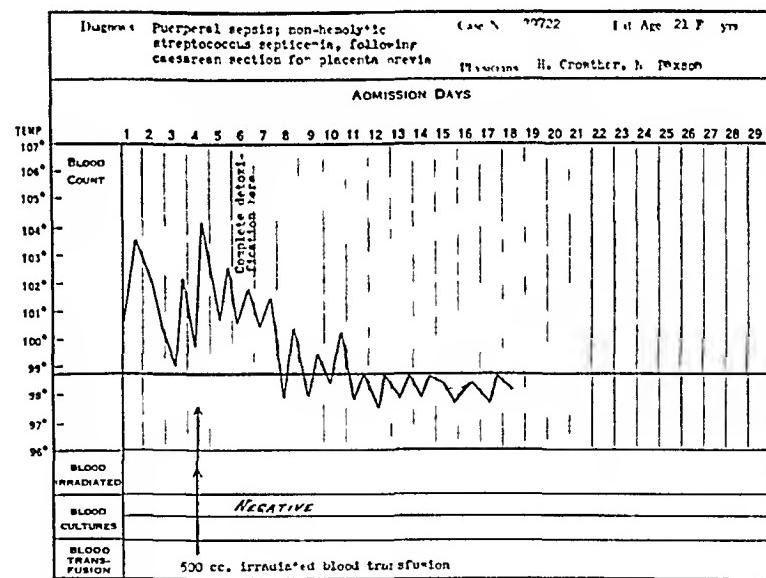
FIG. 3. A, B and C, following exploratory laparotomy in this patient, a ruptured tubal abscess with generalized peritonitis was found. Culture of the purulent peritoneal exudate was found to be Streptococcus hemolyticus; the same organism was found on blood culture. Seventy-two hours after operation, when the patient was apparently moribund, ultraviolet blood irradiation therapy was instituted. Four applications of this therapy were required before detoxification was complete. During this time the abdominal incision had ruptured and evisceration had to be checked by adhesive strapping. The patient recovered, had a secondary abdominal closure, and left the hospital in apparently excellent condition on the thirty-seventh day following the appearance of the final detoxification effect.

constant. These are: (1) the amount of blood withdrawn and irradiated, (2) the time of exposure to ultraviolet energy, and

The amount of blood to be used is calculated from the formula  $A = KW$ , where A is the amount in cubic centimeters



A



B

FIG. 4. A and B, in this girl, aged twenty-one, colored, there developed a markedly severe puerperal sepsis following cesarean section. Despite extensive sulfanilamide and sulfapyridine therapy a non-hemolytic streptococcal septicemia appeared. As a last resort ultraviolet blood irradiation therapy was instituted; the chills disappeared and blood cultures became sterile but sulfapyridine was started again and the patient's condition deteriorated rapidly. This was withdrawn as the patient went into shock and general collapse that was believed terminal. At this time 500 cc. of donor's blood was irradiated and given as no blood could be withdrawn and the patient was apparently moribund. Twenty-four hours later a marked detoxification effect was observable and the patient convalesced uneventfully thereafter.

(3) the intensity and the wave-length of the spectral energy used.

to be withdrawn,  $\kappa$  is a constant (1.5 in this work), and  $w$  is weight expressed in pounds.

The amount of blood used rarely exceeded 300 cc., as can readily be seen from the formula.

The time of exposure is considered to be the time required for the passage of 1 cc. of blood through the Knott irradiation chamber while exposed at contact to the ultraviolet emanation described below; the average time of exposure in this work was ten seconds.

In irradiating blood, ultraviolet wavelengths within the range from 2,399 to 3,654 angstrom units, were used. The intensities corresponding to the wavelengths used are shown in this table:

Wave Lengths, Angstrom Units	Intensities, mW/cm. <sup>2</sup>
2,399	55,000
2,483	88,000
2,536	273,000
2,652	239,000
2,753	86,000
2,804	139,000
2,897	96,000
2,967	224,000
3,022	435,000
3,125-32	718,000
3,342	73,000
3,473	41,000
3,650-54	1,538,000

It can be observed from the above method of estimating dosage and keeping it relatively constant that the fundamental laws underlying the mechanism of photochemical processes have been carefully taken into consideration. The Grotthus-Draper<sup>33</sup> law, known also as the first law of photochemistry, stating that only light which is absorbed can act chemically, the Bunsen-Roscoe<sup>34</sup> law which states that a photochemical change is proportional to the intensity and time of illumination, Stokes'<sup>35</sup> law stating that the wave-lengths of secondary, emitted rays are greater than the primary exciting rays, Einstein's<sup>36</sup> photochemical equivalence law which states that each absorbed quantum should cause one light absorbing molecule to react chemically, and the production of chain reactions<sup>37</sup> by secondary emanations, are all as applicable to biochemical reactions as to chemical reactions in general.

## RESULTS IN CONTROLLING ACUTE PYOGENIC INFECTION

The above described technic of irradiating blood with ultraviolet has been used in 151 cases of acute pyogenic infection as a method of controlling such infection and its toxemic manifestations.

These cases have been classified in three groups, according to the degree of clinical toxicity as follows:

(1) *Early*, in which temperature, pulse and respiratory rates are not greater than 101° to 102°F., 100 to 110 and 24 to 25, respectively, and toxic symptoms such as nausea, vomiting, restlessness, irritability and mental confusion are minimal or absent.

(2) *Moderately advanced*, in which temperature, pulse and respiratory rates exceed 101° to 102°F., 100 to 110 and 24 to 25, respectively, and such toxic symptoms as nausea, vomiting, restlessness, irritability and mental confusion are excessive.

(3) *Apparently moribund*, in which the symptoms present are a combination of those advanced symptoms commonly considered near terminal, or terminal, namely, coma, rapidly falling blood pressure in some instances, cardiac irregularity, irregular and shallow respirations, obvious loss of thermotactic control and often an associated septicemia.

## TABULATION OF RESULTS

This report includes all patients with acute pyogenic infection given ultraviolet blood irradiation therapy at Hahnemann Hospital, Philadelphia, up to January 1, 1942. Of these 151 the majority received no form of chemotherapy, neither before nor after irradiation; a minority were admittedly chemotherapeutic failures.

In Table I we present three classifications of patients suffering from various acute pyogenic infections—according to the severity of the toxic symptoms present at the time of the first irradiation—namely, *early*, *moderately advanced*, or *apparently moribund*.

TABLE I

RESULTS IN 151 CASES OF ACUTE PYOGENIC INFECTION  
GIVEN ULTRAVIOLET BLOOD IRRADIATION THERAPY  
AT THE HAHNEMANN HOSPITAL IN PHILADELPHIA FROM NOVEMBER 1, 1938 TO  
DECEMBER 31, 1941

	No. of Cases	Recover- ed	Died
Early:			
Puerperal sepsis	2	2	
Incomplete septic abortion	2	2	
Acute ulcerative gingivitis secondary to third molar abscess	1		
Acute furunculosis or carbunculosis	2	2	
Acute Streptococcus hemolyticus oropharyngitis	13	13	
Acute tonsillitis	5	5	
Acute pansinusitis	1	1	
Acute tracheobronchitis	4	4	
Acute pyelitis	1	1	
Wound infections	2	2	
Acute otitis media, (diabetes mellitus also in one case)	2	2	
Fever of undetermined origin	1	1	
Moderately Advanced:			
Puerperal sepsis	14	14	
Incomplete septic abortion	14	14	
Pelvic abscesses; pelvic peritonitis	7	7	
Peritonitis, generalized	9	9	
Wound infections	4	4	
Acute femoral thrombophlebitis	4	4	
Acute Streptococcus hemolyticus oropharyngitis	1	1	
Fever of undetermined origin	2	2	
Bronchopneumonia	1	1	
Acute osteomyelitis, advanced nephrosis	1		1
Acute cholecystitis, cholelithiasis	1	1	
Double otitis media	1	1	
Streptococcus viridans septicemia secondary to parotitis	1	1	
Acute suppurative hemorrhagic cystitis	1	1	
Apparently Moribund:			
Puerperal sepsis	2	2	
Incomplete septic abortion	1	1	
Incomplete septic abortion, hemorrhagic shock	2	2	
Peritonitis, generalized	3	2	1
Appendiceal abscess	1	1	
Pelvic abscesses, pelvic peritonitis	6	5	1
Wound infections	3	2	1
Fever of undetermined origin.	2	1	1
Lobar pneumonia	2	1	1
Bronchopneumonia	1	1	
Pyelonephritis, cystitis, secondary to bladder carcinoma	1	1	
Mesenteric thrombosis; large pararectal and gluteal abscess, diabetes mellitus	1		1
Acute extensive phlegmonous ileitis, eecostomy	1		1
Rectal abscesses, cystitis, ileitis, advanced arteriosclerosis	1		1
Bacillus coli abscess of scrotum	1	1	
Streptococcus hemolyticus oropharyngitis complicating mastoidectomy	1	1	
Extensive trauma, terminal bronchopneumonia	1		1
Acute hepatitis and colitis of unknown origin	1	1	
Pelvic abscess secondary to carcinoma of sigmoid	1	1	
Extensive bilateral pyonephrosis secondary to renal tuberculosis	2	2	
Septicemias:			
Staphylococcus aureus	6	6	
Staphylococcus albus secondary to Staphylococcus albus pneumonia	1	1	
Streptococcus hemolyticus	3	3	

TABLE I. (Continued)

	No. of Cases	Recover- ed	Died
<b>Septicemias:</b>			
Staphylococcus aureus and albus septicemia, cavernous sinus thrombosis secondary to eye injury . . . . .	1	..	1
Streptococcus nonhemolyticus . . . . .	2	1	1
Streptococcus viridans subacute bacterial endocarditis . . . . .	6	..	6
Streptococcus nonhemolyticus endocarditis . . . . .	1	..	1
Streptococcus hemolyticus bacterial endocarditis secondary to premature separation of the placenta	1	..	1
<b>Summary</b>			
		Early	Moderately Advanced
Number of cases	35	61	55
Number recovered	35	60	23
Percentage recovered.	100	98	42
Number died	0	1	32
Percentage died	0	2	58

The results of the use of this therapy in the conditions noted are indicated in this Table, which reports, in summary, the recovery of 100 per cent of the *early*, of 98 per cent of the *moderately advanced*, and 42 per cent of the *apparently moribund* (55 per cent nonsepticemic, 19 per cent septicemic) cases. Obviously, the earlier ultraviolet blood irradiation therapy was applied the better were the results obtained.

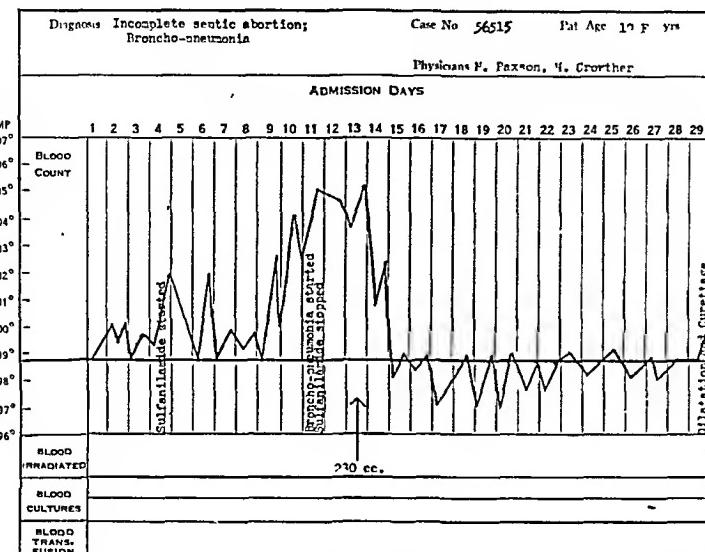
In no case treated by this Knott technic of ultraviolet blood irradiation therapy have there been observed any harmful delayed effects such as deleterious effects on the blood itself, on kidney function nor on any body function. Normal red and white cell count and structure, and normal hemoglobin content is a consistent observation in patients checked up to three years after initial blood irradiation.

Although it is not the purpose of this paper to discuss these effects of this therapy, it may well be added that these findings correspond with those of other workers in this field, e.g., Rebbeck,<sup>38</sup> Knott and Hancock,<sup>32</sup> and Barrett,<sup>39</sup> as well as with our own findings in the more than 500 other patients who have received blood

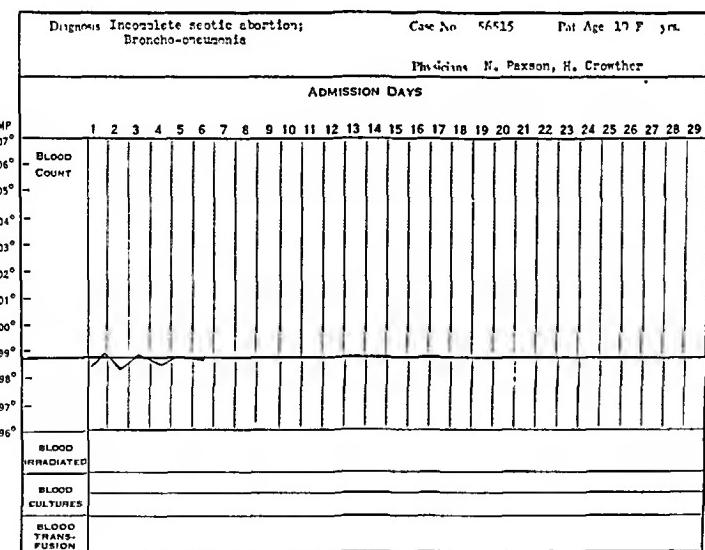
irradiation here for diseases of a more chronic nature.

It is interesting to note that the results

excellent original reports of the use of this method in these two obstetrical complications.



A



B

FIG. 5. A and B, a girl, age nineteen, with incomplete septic abortion, treated with sulfanilamide failed to respond and developed bronchopneumonia. Chemotherapy was wisely abandoned and ultraviolet blood irradiation therapy instituted. Within twenty-four hours the patient's toxic symptoms had subsided and she convalesced uneventfully. Dilatation and curettage was performed two weeks later with a maximum temperature rise to 99.8°F. The patient was discharged six days later, three weeks after ultraviolet blood irradiation therapy.

obtained in using ultraviolet blood irradiation therapy as a control of infection in cases of puerperal sepsis and incomplete septic abortion very closely parallel the results reported by Rebbeck<sup>38</sup> in his

#### ABSTRACTS OF FOUR TYPICAL CASE HISTORIES

For the purpose of a more detailed observation of the results of this treatment there follows a series of brief abstracts of

case histories of a few selected cases from Table 1:

T. G., No. 69618, a fifty-six-year old white

The legs were covered with a heat cradle and elevated on pillows. Dilaudid gr. 1/16 was necessary to control the pain; 150 cc. of

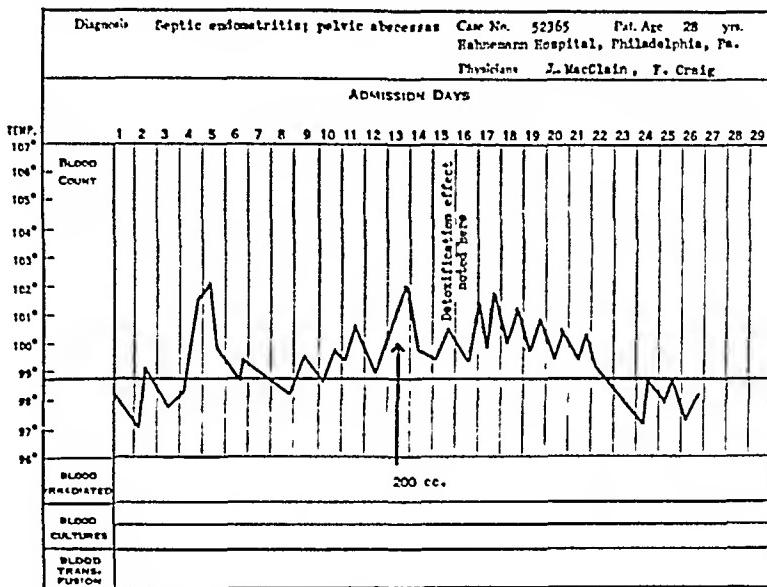


FIG. 6. Septic endometritis and pelvic abscesses in this woman produced, on the thirteenth hospital day, rapidly progressing toxic symptoms. Ultraviolet blood irradiation therapy was instituted immediately, and detoxification was complete in forty-eight hours, though her temperature remained elevated till the twenty-second day, falling to normal at that time. The patient in fairly good condition, signed herself out of the hospital four days later against the advice of the staff.

male, was admitted to the Hahnemann Hospital complaining of pain in both feet. Examination of his feet revealed a dry gangrene of the right great toe and a swollen tender area on the medial side of his left heel. Both ankles were swollen. On May 14, 1941 neither tibial nor dorsalis pedis pulses were palpable. The patient gave a history of having had his feet frozen several times in the last ten years. During the past summer the patient apparently had symptoms of intermittent claudication. In November, the patient noticed that the right great toe was sore and this continued until April, 1941, when he injured this toe and it became infected. The toe was incised to establish drainage but the toe only became worse and turned black. He came to the accident ward seeking help and was admitted on May 14, 1941. The urinalysis, blood count, blood sugar and blood urea were all normal. Wassermann and Kahn tests were normal. Blood culture was sterile after 120 hours' incubation. Temperature was relatively normal except for a small rise in temperature to 99°F. each evening. Treatment was instituted as follows:

5 per cent saline were given daily for three days and then three times weekly. On May 16, 1941 the vacuum pressure boot was started on both legs. The saline and the boot seemed to aggravate the condition so that they were stopped on May 22, 1941 and the patient was advised amputation of the right leg above the knee because of the mortification setting in half way to the right knee. On May 25th under cyclopropane-oxygen anesthesia the right extremity was amputated just above the knee using the guillotine method. Good hemostasis was obtained, the flaps approximated and the incision closed with drainage.

Following this operation the patient was very much improved and had very little discomfort. The sutures and drains were removed May 31st and the patient was ordered out of bed. Dressings were changed daily.

On June 12th the patient began to complain of the left heel which had apparently been healed. Whirl-pool bath was ordered daily. The patient then began having pain in the stump and the heel and on June 15th a nerve block was ordered. Since the whirl-pool bath

apparently aggravated this pain, it was discontinued.

On June 17th a lumbar sympathetic nerve

formed June 27th. Following this irradiation the swelling went down in the left foot and the area on the left heel began to heal and granu-

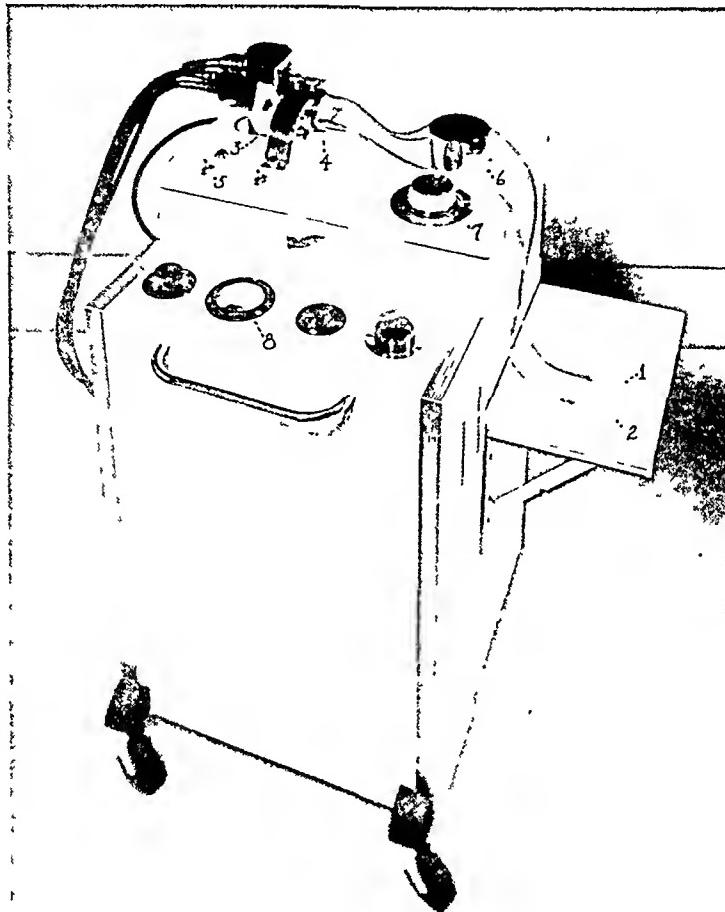


FIG. 7. Blood irradiation machine (hemo-irradiator). 1, glass-tipped adapter for the suction or withdrawal end of the rubber tubing system. 2, glass-tipped adapter for the intravenous or injection end of the system. This is fitted to a needle in the patient's vein. Citrated blood that has just passed through the irradiation chamber (4) and thus irradiated is returned to the venous circulation through this adapter. 3, water-cooled, mercury-quartz burner, the source of high intensity ultraviolet energy used in irradiating blood. 4, Knott irradiation chamber with quartz window held in contact with mercury-quartz burner. Blood is passed through this chamber, its time of exposure being carefully and automatically adjusted. 5, hemo-irradiator starting switch. 6, synchronized transfusion pump. 7, dial regulating rate of flow and time of exposure. 8, voltmeter.

block was done; just before the block an abnormally high skin temperature was recorded. The patient was not relieved of pain and the temperature of the leg did not change. This was repeated on the 19th without relief to the patient. The patient complained almost constantly of pain in the left heel which had now become swollen and edematous. Pain continued until blood irradiation was per-

late. The stump of the right leg was almost completely healed following this and the drainage was negligible.

On July 3rd the patient was discharged free of pain both in the right amputation stump and in the left heel, along with slight drainage from the left heel and the stump of the right leg.

E. J., No. 69619, a twenty-two-year old black female, was admitted to the hospital on August 20, 1941. The diagnosis was Streptococcus hemolyticus septicemia and generalized peritonitis secondary to ruptured tubo-ovarian abscess. On admission she was complaining of severe abdominal pain and gave a history of sudden onset. Physical examination revealed a markedly tender, rigid abdomen characteristic of an acute intra-abdominal condition. Her pulse was 110, respirations 30, temperature 101°F. Pelvic examination revealed presence of fluid in the cul-de-sac. Laboratory examinations revealed negative urinalyses, hemoglobin 14.3 Gm., red cells 4,700,000, white cells 12,300. A diagnosis of ruptured ectopic pregnancy was made and laparotomy was performed soon after admission of the patient. At operation generalized peritonitis was found which was obviously due to a ruptured tubo-ovarian abscess. The abdomen was closed with adequate drainage and aldonil was given. The patient's temperature, pulse and respirations rose to 105°F., 140 and 36, respectively. Sulfathiazole was started the second postoperative day, August 22nd; the patient became extremely nauseated and vomiting appeared; her condition was grave. Sulfathiazole was stopped. Twelve hours later ultraviolet blood irradiation therapy was instituted, August 23rd. At this time blood culture taken on the day of admission was found to be positive, showing a pure and luxuriant growth of Streptococcus hemolyticus. The next forty-eight hours the patient seemed generally improved, temperature, pulse, respirations falling to 99°, 102 and 30, respectively.

On August 26th, the wound began to break down and the following day, because of a rise in respiratory rate to 38, ultraviolet blood irradiation therapy was repeated. The following day the temperature continued to rise as did the pulse and respiration, to 103.2°F., 148 and 46, respectively. On August 29th a third blood irradiation was administered.

On August 29th x-ray examination of chest failed to show any definite pulmonary disorder but the patient was put in an oxygen tent because of marked dyspnea and the presence of râles throughout the chest. The patient's condition remained stationary and on September 2nd ultraviolet blood irradiation therapy was given for the fourth time. The following day her temperature rose to 105°F.; forty-eight

hours later it began to fall. At this time, September 4th, it was believed that the oxygen tent should be removed because of the apparent deleterious effects of mechanical irritation and overventilation. On removal of the oxygen tent respiratory rate fell to a level between 24 and 30. Shortly after this a large, subcutaneous and subfascial abscess ruptured. On September 6th the patient was definitely out of danger and continued to convalesce uneventfully till October 4th when her temperature rose to 101.2°F. There was a daily temperature rise to 101° or 102°F. for three days following, during which time an inflammatory area appeared in the lateral region of the left buttock. On October 17th this ruptured and her temperature fell to normal. The patient convalesced uneventfully from this point on and was discharged in good condition on November 2nd.

A. W., No. 69406, a twenty-year old white female, finally diagnosed as having puerperal sepsis and septic endometritis complicated by acute pyelitis, was admitted to the obstetrical ward November 24, 1941 at full term. Mid-forceps delivery was performed; third degree lacerations of the peritoneum occurred. The first four days following delivery the patient ran a moderately septic course, temperature ranging from 100° to 103°F. On the fifth postpartum day, her temperature, pulse, and respirations rose to 105.8°F., 138 and 34, respectively; severe chills were present; urinalysis showed 30 to 40 pus cells per H.P.F. The chills continued for forty-eight hours; the patient became nauseated, delirious and increasingly toxic. On the seventh postpartum day, ultraviolet blood irradiation therapy was instituted. The following day no chills occurred, nausea was absent, the patient was mentally alert, and her temperature, pulse and respiration fell to normal levels; her toxic symptoms had generally subsided. This improvement was maintained with the result that she convalesced uneventfully, leaving the hospital on the seventeenth postpartum day, in apparently excellent condition, ten days after a single irradiation.

S. C., No. 65978, a white woman of fifty-two years was admitted to Hahnemann Hospital on August 11, 1941. The final diagnosis was incomplete septic abortion complicated by lobar pneumonia. When admitted she was complaining of chills, fever and abdominal bleeding,

giving a history of approximately ten days of chills and fevers. Physical examination revealed a markedly toxic patient with a temperature of 103° F., pulse 120, respiratory rate of 20. Pelvic examination revealed a lacerated external os and vaginal bleeding. Laboratory examination revealed hemoglobin 11.2 Gm., red cell count 4,000,000, white count 12,250, sedimentation rate 7 mm. in fifteen minutes, 30 mm. in forty-five minutes; culture of the cervix showed the presence of *Staphylococcus aureus* and *Bacillus diphtherodeus*. Sulfathiazole was started immediately on admission. Within a few hours her respiratory rate rose to 40 and some cyanosis was present. The following day an x-ray examination of the chest, showed the presence of consolidation characteristic of early lobar pneumonia. The patient's general condition continued to deteriorate, her dyspnea and cyanosis increased, mental confusion, nausea and vomiting appeared and her temperature (Fig. 1), pulse and respiratory rates remained elevated. Therefore, because after seventy-two hours of sulfathiazole therapy it was believed that the patient's condition had been in no way improved by sulfathiazole, and that, on the contrary, it had become very critical, sulfathiazole was discontinued. Several hours later ultraviolet blood irradiation therapy was instituted; within a few minutes the patient's dusky cyanosis began to disappear and in its place was seen a definitely pinkish skin coloration, a grossly discernible peripheral flush (which, incidentally, persisted up to the time of her discharge). On the following day the patient's temperature began to fall, as did her pulse and respiratory rate; her mental confusion, nausea, vomiting and dyspnea disappeared. This marked detoxification effect was most striking. Forty-eight hours later, pulse, temperature and respirations were normal and the patient was obviously out of danger. She convalesced uneventfully and left the hospital on August 25th, ten days after a single blood irradiation.

In order to show a more detailed picture of the effect of ultraviolet blood irradiation therapy on septic temperatures, a series of graphs of daily peak temperatures selected from cases reported in Table 1 (Figs. 1 to 6) are shown. These are typical of the whole group presented in this paper. As might be

expected, abnormally high temperatures fell both by lysis and by crisis.

#### GENERAL CLINICAL OBSERVATIONS

During this work several rather outstanding clinical events were noted, and their relation to the known physiological effects of ultraviolet mentioned earlier in this paper have been correlated insofar as possible. These may best be summarized as follows:

1. The bactericidal effect has been noted throughout this work. A complete disappearance of the invading bacterial organism was found to occur except in cases of *Staphylococcus aureus* septicemia and in cases of acute or subacute bacterial endocarditis.
2. The detoxification effect has been the most striking of all effects observed in cases of acute pyogenic infection following ultraviolet blood irradiation therapy. There occurs in these cases almost uniformly, twelve to seventy-two hours following this therapy, a pronounced subsidence of toxic symptoms, such as nausea, vomiting, delirium, fever, general malaise, rapid pulse, rapid respiration, etc. In this connection we have observed that there often occurs a marked fall in abnormally high temperatures by lysis or by crisis. If, however, abscess formation is present or occurring the abnormally high temperature will drop to a level slightly above normal; in such cases all toxic symptoms usually disappear and the elevated temperature drops to normal upon drainage of the abscess. In fact, we have found a disappearance of toxic symptoms in combination with a slightly elevated temperature following ultraviolet blood irradiation therapy to be pathognomonic of abscess formation. In bronchopneumonia the temperature has been observed to fall by lysis.
3. Grossly discernible peripheral vasodilation has been observed in over 75 per cent of all individuals given ultraviolet blood irradiation therapy. This occurs within five to ten minutes after the irradiated blood has been returned to

the venous circulation and persists in some individuals for more than thirty days.

4. Photosensitization and photodynamic effects have been carefully considered in this work, although there is neither time nor space here to present these studies. We have made a few fundamental observations regarding the combined use of chemotherapeutic agents, especially sulfanilamide derivatives, quinine and iodides with ultraviolet blood irradiation therapy. These are, briefly: (a) Ultraviolet blood irradiation therapy can be given safely and with impunity following the administration of sulfanilamide derivatives, quinine and iodides; (b) sulfanilamide, sulfapyridine and iodides cannot be given safely within the first five days following ultraviolet blood irradiation therapy without risking a probable photosensitive reaction in the form of markedly increased toxemia, pulmonary edema and renal shut-down. In the one case of photodynamic action observed with sulfathiazole (given seven days after ultraviolet blood irradiation therapy) marked convulsions were seen; no serious effects have been seen with the administration of quinine in the first few days following this therapy; (c) those patients who have only blood irradiation have a much shorter convalescent period than those who receive both sulfa drugs and ultraviolet blood irradiation therapy.

5. The ability of ultraviolet irradiated blood to absorb oxygen has been studied<sup>18</sup> and in this work it was found that in patients with abnormally low venous oxygen values who received ultraviolet blood irradiation therapy, there was a marked increase in the uptake of oxygen as shown by a definite rise toward normal of venous oxygen values.

6. Secondary emanatory phenomena present difficult problems for careful analysis. At this time no statement can be made. Knott was able to fog a photosensitive film in a dark-room with the serum of blood irradiated according to the above described technic.

7. General resistance, as may be ex-

pected in the light of the previously mentioned observations, was obviously increased.

8. A complete absence of deleterious effect has been noted in this work. Earlier it was reported<sup>10</sup> that in individuals with initially normal red cell, white cell and hemoglobin values there was observed to be little, if any, change one to thirty-six months following ultraviolet blood irradiation therapy carried out strictly in accordance with the technic and dosage described above. Similarly, we may add that in patients receiving blood irradiation for acute pyogenic infection and having abnormal hemoglobin, red cell and white cell values before treatment all these disappear, changing to normal following hemo-irradiation. We have been unable to find delayed harmful effects of any nature in well over 1,000 applications of the Knott technic of ultraviolet blood irradiation.

Up to the time of the writing of this paper, in the treatment by blood irradiation of cases of acute pyogenic infection uncomplicated by septicemia we have never seen an infection progress to the point where a septicemia has ensued.

We have often seen, as have others, a complete failure of chemotherapeutic agents insofar as controlling the infection is concerned. Many of these cases have responded to ultraviolet blood irradiation therapy subsequent to chemotherapy failure. We have yet to witness a case in which ultraviolet blood irradiation failed and chemotherapy succeeded.

The above clinical observations are in close agreement with those made by others working with the Knott technic of ultraviolet irradiation of blood, notably Hancock,<sup>32</sup> Rebbeck<sup>38</sup> and Barrett.<sup>39</sup>

#### SUMMARY

1. A method of irradiating human blood, originally devised and recently modified by Knott, is described. This consists of withdrawing and retransfusing a predetermined amount of a patient's venous blood and immediately returning it intravenously

through a closed system containing a Knott irradiation chamber at which point intense ultraviolet irradiation is applied.

2. The amount of blood used (predetermined according to approximate body weight), the time of exposure (optimally ten to twelve seconds in the treatment of acute pyogenic infections), and the wavelengths and intensity of the spectral energy used form the basis for estimating and maintaining a relatively constant dosage.

3. A report of 151 cases of acute pyogenic infection treated at Hahnemann Hospital over a period of three years is given; the clinical response has been consistently excellent.

4. A rapid subsidence of toxic symptoms with subsequent recovery in all of the early cases, all but one of the moderately advanced cases, and in some of the apparently moribund cases of acute pyogenic infection was found to occur. Other beneficial physiological effects, e.g., bactericidal effect, vasodilation, venous oxygen increase, were observed to occur following this therapy.

5. As yet, no case of acute pyogenic infection uncomplicated by septicemia, after receiving ultraviolet blood irradiation therapy according to the Knott technic, has progressed to a septicemia.

#### CONCLUSIONS

1. The Knott technic of irradiating blood with ultraviolet must be considered, in view of the method of its administration and of the various physiological effects it produces, as a method of applying ultraviolet energy intravenously.

2. This method has been found to be valuable for controlling acute pyogenic infections rapidly and efficiently. The earlier it is applied in the course of an acute pyogenic infection the better have been the results obtained.

3. The technic described is essentially a hospital procedure at present. It requires careful training in its use and when properly administered is without harmful after-effects.

4. Experience with the Knott technic of irradiating blood has convinced us that when available it offers more to the patient suffering from acute pyogenic infection than any other therapy yet known.

5. As a control of infection it is the obvious method of choice in those cases of acute pyogenic infection in which chemotherapy has failed.

6. In general it may be said that wherever a bactericidal, detoxification or vasodilation effect is needed, as well as such other physiological effects of ultraviolet as increased ability of the blood to absorb oxygen and increased general resistance, the Knott technic of ultraviolet blood irradiation therapy is indicated.

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In the sterile uterus there should be no hesitancy in performing vaginal hysterectomy both to relieve the active symptoms and also from a prophylactic standpoint.

# EMBOLISM OF THE PERIPHERAL ARTERIES\*

## REPORT OF SIX CASES

ARTHUR M. DICKINSON, M.D.

Chief Surgeon, Memorial Hospital

ALBANY, NEW YORK

THE condition of embolism of the peripheral arteries has been recognized for years. The first attempt at surgical removal of such an embolus was made in 1895. The first successful embolectomy was performed in 1911, by Labey or Key. Since that time operative attacks upon peripheral emboli have been made with considerable frequency, particularly in the Old World and especially in Britain and Sweden. In the medical literature of these countries there appear frequent discussions as to technic of operating along with many case reports. The American literature on the other hand does not contain such frequent reference to this condition.

There are several factors which play important rôles in the lodgment of emboli in peripheral arteries and of these, three are more or less constant. These factors are the heart factor, the arterial factor and the precipitating factor. The first or heart factor is practically always present and usually is in the form of valvular disease, rheumatic heart disease or mural thrombi. The second, or arterial factor, is not always present. This is usually in the nature of arteriosclerosis or endarteritis and is obviously of considerable importance in the older group of patients. The third, or precipitating factor, is always present although variable. The most common of these is auricular fibrillation for any change in the rhythm of the heart may result in the loosening of a pre-existing vegetation from one of the valves or from the endocardium. Surgical operation, with the accompanying shock, etc., may be a precipitating factor. Systemic diseases, such as diabetes, nephritis, acute infections, etc., are likewise of importance in this respect.

Peripheral arterial emboli show a marked tendency to lodge at the site of bifurcation or at a point where a major branch is given off. The frequency of involvement of the various vessels is given as follows:

	Per Cent
Bifurcation of the aorta	4 5
Iliac artery	17 0
Femoral artery	55 0
Popliteal artery	11 0
Braehial artery	12 0

Commonly two types of emboli are encountered. The first is the simple type limited to the lumen of a single vessel and extending upward and downward in that vessel from the site of bifurcation to a major branch for a variable distance. The other type is the so-called rider or saddle type in which the embolus extends peripherally from the point of division along both branches. Once an embolus has lodged, secondary thrombus formation takes place due to deposition of fibrin and blood cells and so the color will vary depending upon the type of cells caught. As this thrombus increases in size, it may extend a considerable distance and occlude collateral vessels also. In addition, local reactive changes in the intima occur, thereby fixing the embolus.

The immediate effect of the lodgment of an embolus will depend upon whether there is partial or complete stoppage of the artery involved. If at first it is partial, this soon becomes a complete stoppage due to secondary thrombus formation. As a result of the greatly diminished blood supply, tissues of the area suffer from anemia and anoxemia and harmful metabolites accumulate. Gangrene may or may not develop depending upon the extent of collateral circulation. That this is an important

\* From the Surgical Service at the Memorial Hospital, Albany, New York.

factor is illustrated well by the knowledge that gangrene does not commonly follow sudden occlusion of the brachial or axillary arteries, while a similar process in the popliteal is almost certain to produce gangrene. In addition to these local changes, there are more remote effects resulting from reflex vasospasm. Due to irritation of the endothelial lining at the site of embolism, presser stimuli transmitted through the sympathetics cause contraction of the other arteries nourishing the limb, thereby further decreasing the blood supply.

The symptoms of peripheral arterial embolism are quite characteristic, the more important of them being: pain, pallor, paralysis, absent pulsations and temperature changes.

Of these pain is perhaps the most important; it is usually sudden of onset, severe and agonizing. The location of the pain does not, as a rule, indicate the site of lodgment of the embolus at first; later on the pain is more definitely referred to the part involved. For example, in embolism high up in the femoral artery, pain is usually felt first in the heel or foot. Pallor of the involved limb is quite striking. The limb soon appears wax-like and shrunken. Above the level of pallor, one often finds small petechial hemorrhages into the skin. Paralysis of both motion and sensation come on quite promptly after the onset. At first, only the finer movements and epicritic sensations are lost; later the coarser movements and protopathic sensations disappear. Obviously, pulsations in the artery distal to the site of embolism will be absent. Ordinarily, this can be determined by simple palpation. It can be further checked by using an aneroid type of blood pressure apparatus and comparing the oscillations at corresponding levels on both limbs. The oscillograph will quickly indicate the difference in excursion but is not essential. Temperature changes are manifest promptly after the onset. These can be readily appreciated by palpation for the sensitivity of the finger tips is usually sufficient to detect differences of more than

one degree. A more accurate recording can be obtained by use of skin thermometer or a thermocouple.

The outcome in cases of peripheral arterial embolism depends upon many factors. The most important of these, from a surgical viewpoint, is the time interval, by which is meant the elapsed time between lodgment and institution of treatment. Patients operated upon within eight hours, show a surprisingly high percentage of good results. If, on the other hand, operation is delayed beyond the twenty-four-hour period, results are very poor. Obviously, the general condition of the patient is an important factor also. If the heart is severely diseased, or future emboli are thrown out from the heart to lodge in other important vessels, the prognosis is bad. The presence of adequate collateral circulation, and the absence of advanced arterial disease, likewise contribute to a successful outcome. These factors are particularly important in older persons. According to Key, cures may be obtained in the following percentage: Brachial-axillary, 44 per cent; femoral, 20 per cent; popliteal, 20 per cent; aorta, 17 per cent; iliac, 15 per cent. The accessibility of the involved artery is always a factor in influencing the eventual outcome. This is self evident. Damage to the intima by the embolism, or by the surgeon at operation, decreases the chances of a satisfactory outcome. In general, the following figures illustrate the percentage of cures obtained in a large series of cases. Key, of Sweden, reports 38 per cent cures by operation; Lund, of Boston, reports 37 per cent cures by operation. Inasmuch as these figures are quite parallel, we may assume that they represent the average experience. Lund, on the other hand reports only 10 per cent of cures in a series of patients not operated upon.

Treatment may be divided into that by medication, by physical agents and by surgery. Vasodilators are apparently of some value, particularly nitrates, belladonna or its alkaloids, opiates in various forms, etc. Of all of these, spasmalgin, which is a

combination of pantopan, papaverine, and atrinol, is the most satisfactory for the reason that it allays pain and helps to eliminate vasospasm of the other vessels. Heparin may be of some value in the treatment of these cases. It will not dissolve existing emboli, but diminishes further thrombus formation. At present the use of heparin is not general, because of the expense of the drug, and because of the fact that it must be given by a continuous intravenous drip over a period of one or more days and is rapidly eliminated through the urine. Furthermore, the administration of heparin of considerable quantity, so depresses coagulation that bleeding from the operative wound may occur. Heat often gives these patients considerable relief and may be a factor in recovery. Heat may be applied in the form of hot water bottles, electric pads, electric cradles, etc. Great care not to burn the patient is needed for high temperatures do more harm than good. The Pavex machine is certainly of definite value in the establishment of the collateral circulation. The same may be said of the intermittent venous occlusion machine. With some patients, however, they seem to increase pain. Modified Buerger exercises also may be helpful. Ordinarily, however, there is very little time for trying out medical treatment or physical agents and surgery is undertaken promptly. The statistics given above quoted from Lund, plainly indicate the superiority of surgery over all other methods of treatment for this condition.

The choice of the anesthetic agent is largely a personal problem and must be left to the judgment of the operator and the anesthetist. However, if the operation can be done under infiltration anesthesia or spinal anesthesia, the patient may be saved the dangers attendant upon the administration of a general anesthetic agent.

In operating for removal of an embolus of a peripheral artery, adequate experience is essential here just as in any other operative procedure. Work is greatly facilitated by having a sufficiently large incision.

Control of bleeding from the vessels to be attacked is an important problem, especially if the vessel is one of the large ones. Soft rubber covered clamps are applied above and below the prospective site of incision of the vessel. When the vessel involved is a large one, it has been my policy to throw a wide tape around the vessel above the proximal clamp so that if inadvertently the clamp slips, the tape can be tightened by an assistant, thereby preventing the sudden loss of a considerable amount of blood. Throughout the operation, the wound, and particularly the vessels should be kept moistened continuously with either normal saline or citrate solution. Before incising the vessel it is wise to strip off the adventitia which accomplishes two purposes: First, it interrupts the sympathetic nerve fibers, and thereby diminishes considerably the vasoconstrictive reflex exerted on the collaterals. Secondly, it facilitates subsequent suture of the vessel wall by eliminating the adventitia which has a tendency to curl in the wound. The point of incision into the vessel should be carefully chosen; it should be either above or below the site of lodgment of the embolus, never directly over it. As we know, emboli tend to cause changes in the intima, and if the intima is further damaged by incision at this location, there is an increased possibility of secondary thrombus formation after an otherwise successful operation. In removing the embolus, care must be exercised not to injure the intima by sharp instruments. Various types of long alligator forceps have been devised for this use which are capable of being passed several inches along the lumen. I have frequently used a rubber catheter and attached syringe to aspirate the embolus which method seems to offer less chance of injury to the intima. At the same time smaller fragments may be washed out by injecting saline or citrate solution. After the embolus has been removed, the clamp on the proximal side is released, which demonstrates clearing of the lumen and flushes out any small particles. The clamp is then replaced and

the distal clamp loosened with the same purpose. The distal segment is treated in a similar manner as was the proximal segment, utilizing a catheter and syringe. If there is any doubt as to the patency of the vessel distally, injection of saline will promptly settle the question.

When one is satisfied that the lumen of the vessel is clear, clamps are replaced, and repair of the vessel wall is done with fine waxed silk and a small needle, utilizing the technic laid down by Carrell. Frequently, after the suture is completed and the clamps removed, there is a little bit of oozing at one or more points. This usually can be controlled by temporary pressure with cotton, or the application of a small bit of muscle. At the completion of the operation, the limb is splinted to prevent any sudden movement and strain upon the vessel.

To date, I have operated upon six patients with embolism of the peripheral arteries. All of these patients were males. Three of the patients were more than sixty years of age, two were about forty-five, and one was thirty-two. The frequency of involvement of the various vessels was as follows: femoral, two; popliteal, two; brachial, one; common iliac, one. In the series there was one successful outcome and five failures. All of these five came to amputation. One death followed amputation.

#### CASE REPORTS

**CASE I.** F. J. P., male, age sixty-two, entered the hospital complaining of pain, pallor and paralysis of the right leg of about twenty-four hours' duration. He had a hypertensive heart disease with mitral regurgitation. The entire right leg from the knee distally was white, cold and paralyzed. Pulses of the femoral arteries were equal on both sides. The left popliteal artery pulsated normally. Pulsation of the right popliteal was absent. Under spinal anesthesia the right popliteal space was opened and the popliteal artery exposed and found pulsating. It was then explored downward to the point of bifurcation, beyond which both branches were occluded. Embolectomy was done with the finding of a rider type of em-

bolism which we thought we removed entirely. Following operation, however, pulsation did not return to either the dorsalis pedis or the posterior tibial arteries and the leg went on to ultimate gangrene in about two weeks. Amputation was followed by an acute heart episode and terminated fatally. Examination of the vessels of the amputated leg showed advanced arteriosclerosis with thrombosis of the vessels in the middle third of the leg.

**CASE II.** A. D., male, age forty-five, entered the hospital complaining of pain, pallor and paralysis of the left leg of twenty hours' duration. Examination showed an enlarged heart with no murmurs. Electrocardiograph revealed evidence of considerable myocardial damage. The left leg was cyanotic and cold. Pulsation of the left femoral artery appeared normal, but no pulsations of the left popliteal artery could be determined. There was tenderness in the left popliteal space. Under cyclopropane anesthesia the left popliteal space was explored and the popliteal artery examined. Incision into the vessel was followed by removal of an embolus about eight inches in length. Following removal of the embolus, there appeared to be temporary improvement with restoration of the pulsation of the dorsalis pedis artery. Four days after operation there were signs of beginning dry gangrene of the extremity. Eight days following the embolectomy, amputation of the lower third of the thigh was done. Examination of the vessels of the amputated leg showed arteriosclerosis of the Monekeberg type. Also there were emboli of anterior tibial and dorsalis pedis vessels in the lower third of the leg.

**CASE III.** B. C., male, age sixty-six, entered the hospital stating that three hours previous to admission he had been seized with a severe pain in his right thigh while fishing. The leg shortly became useless and numb. The heart was enlarged but no murmurs could be heard. The right thigh showed discolored areas in the upper third below which the extremity was white and cold. The right femoral artery could be felt pulsating in Scarpa's triangle, but pulsation of the right popliteal artery was absent. With the oscillometer no excursion was found in the lower third of the right thigh in contrast to a reading of 12 for the left thigh. The reading of the right calf was likewise zero, whereas that of the left was 6. Under the impression that there was an embolus of the common femoral artery at the site of origin of the pro-

funda femoris, exposure was made in Scarpa's triangle with spinal anesthesia. At the level of the inguinal ligament, pulsations of the femoral artery were evident but lower down they were absent. Incision into the vessel was done with the removal of a three-inch embolus. On the day following operation, the entire leg was warm and sensation was present as far distally as the level of the ankle. With the oscillometer, however, we obtained zero readings below the middle of the calf. Condition of the leg and foot appeared to be improving until the fourth day when the patient's heart decompensated. This was controlled but by the seventh postoperative day beginning gangrene of the lower leg was noted. About fourteen days later, amputation was done four inches below the knee with ultimate recovery of the patient. Examination of the vessels of the amputated leg showed a Monckeberg type of sclerosis with an extensive thrombosis of all of the vessels.

CASE IV. J. C., male, age thirty-two, entered the hospital complaining of severe pain, numbness, and loss of function of the right arm of ten hours' duration. Examination showed a pale, cold, pulseless right upper extremity. This patient had a quiescent pulmonary tuberculosis. Under infiltration anesthesia with novocain, the brachial artery was exposed in the upper arm and a two-inch long embolus removed. Circulation appeared to be restored locally but the radial pulse did not return. Ultimately, gangrene developed and fourteen days later, amputation of the middle third of the arm was done from which the patient recovered promptly. The vessels of the arm showed little except extensive areas of thrombosis.

CASE V. J. T., male, age forty-three, entered the hospital complaining of numbness and pain and loss of use of the right leg of five hours' duration. He was a known cardiac and had been fibrillating for several days. The right leg was cold and white below the level of the knee. There was loss of tactile and temperature sensation also. Pulsation of the right popliteal artery was not felt; that of the left was present. It was thought that pulsations of the right femoral artery were present. Under the impression that the embolus was located in the distal portion of the deep femoral or popliteal arteries, exposure was done through a posterior incision. The popliteal artery was opened and did not bleed upon release of clamps. Suction with a catheter placed proximally produced

nothing. This wound was then closed and the femoral artery in Scarpa's triangle explored. The upper part of the vessel pulsated but the distal segment did not. Incision with removal of a long thrombus was done. Postoperatively, the patient's general condition was only fair, being complicated by the primary heart condition. However, the right leg regained color and sensation and became warm, but pulsations of the vessels were not detected. About nine days after embolectomy gangrene of the leg was definite and subsequent amputation above the knee was successfully carried out. Dissection of the vessels of the leg revealed generalized arteriosclerosis and thrombosis of the popliteal artery.

CASE VI. J. T., the same patient as in Case v, about twenty-three days later, developed numbness, coldness and loss of use of the remaining left leg. No pulsations of the femoral artery or distal thereto were made out. The oscillometer gave a zero reading with the cuff applied to the midthigh region. A diagnosis of embolism of the external iliac artery was made and this vessel was exposed through a lower left abdominal incision, using spinal anesthesia. The site of embolism was found to be at the bifurcation of the left common iliac artery. The left common iliac artery was incised and an embolus about 2 inches long removed. Pulsations reappeared in the palpable vessels distally and circulatory balance was gradually restored. Apparently, a small clot must have blocked off a branch of the anterior tibial artery for subsequently a small superficial area below the knee became gangrenous. This patient lived several months and finally died from acute heart failure.

#### CONCLUSIONS

1. The literature on arterial embolectomy has been reviewed, and the essential parts of etiology, pathology, symptoms and treatment are given.
2. Surgical removal of the embolus gives the patient the most hope of a satisfactory result.
3. Early operation and careful technic are essential if a satisfactory outcome is to be secured.
4. The author reports six instances of arterial embolectomy from his own practice with one recovery, and this in a case of embolism of the common iliac.

# HASHIMOTO'S DISEASE (STRUMA LYMPHOMATOSA)\*

E. C. MOORE, M.D. AND O. DALE LLOYD, M.D.

The Moore-White Clinic

LOS ANGELES, CALIFORNIA

**A**N occasional diagnostic error is often compensated, not only because it may become an incentive for further reasoning and investigation, but also because it should eliminate the danger of a diagnosis based upon superficial routine examination. This danger is particularly applicable to diseases of the thyroid gland especially in the absence of toxic symptoms.

Riedel,<sup>1</sup> in 1896, described woody thyroiditis. He stated that this condition was characterized by marked fibrosis of the thyroid and surrounding structures to such a degree that surgical removal of the involved gland was impossible.

In 1912, Hashimoto<sup>2</sup> reported four cases of chronic thyroiditis occurring in females aged forty to sixty-one years. The pre-operative diagnosis was adenoma or carcinoma of the thyroid. He found, however, that although the microscopic findings were similar to those described for iron-hard struma, the gland separated easily from surrounding structures at operation, bleeding was slight and there was no involvement of adjacent structures. He concluded that, despite some similarities to Riedel's thyroiditis, he was in reality dealing with an entirely different disease entity which he termed "struma lymphomatosa."

A positive clinical diagnosis of Hashimoto's disease is practically impossible to make<sup>3,4,5</sup> and gross examination of the goiter at operation may easily mislead the surgeon in his diagnosis. It remains for the pathologist to differentiate, especially when the clinical findings suggest carcinoma or Riedel's struma, the two conditions most likely to be confused with Hashimoto's disease.

## CASE REPORT

Mrs. B. F., aged fifty-three, married for the fourth time and nulliparous, was first seen on January 3, 1940. She complained of a lump in her throat toward the left side of two weeks' duration, tightness in her chest and palpitation of the heart. She recalled having had a similar *enlargement in April, 1939, but this was a transitory symptom.*

In childhood she had measles, mumps, pertussis, scarlet fever and diphtheria with no complications. Tonsillectomy was performed in 1916. In 1925, a pelvic abscess was drained through an abdominal incision. A one-plus blood Wassermann was found in 1937 at which time she received several injections of bismuth. The menopause appeared at forty-five and there have been no untoward symptoms since, except nervousness and mild insomnia.

Physical examination revealed a well nourished white female. The temperature, pulse and respirations were normal and blood pressure was 130/80. There was a diffuse, rather hard and nodular enlargement of the thyroid. Heart, lungs and vocal cords were normal. A firm lower midline abdominal scar was noted. Other physical findings were negative.

Urinalysis showed a trace of albumin, a few leucocytes and erythrocytes but no casts. Blood count was normal. Blood Wassermann was three-plus, the Kline test two-plus. Basal metabolic rate was plus ten. X-ray of the chest showed no abnormalities. The patient was given a total of four injections of bismuth over a period of three weeks.

A total thyroidectomy was performed on February 3, 1940, leaving a small portion of capsule near the trachea on either side with the hope that one or more parathyroids would be preserved. The postoperative course was uneventful except for slight carpopedal spasm on the second and third day. This disappeared on administration of parathormone and calcium gluconate, and the patient was discharged on

\* Presented before the Los Angeles Surgical Society, December 13, 1941.

the eighth day in good condition. She is now taking 3 gr. of thyroid extract daily and has resumed her antiluetic therapy. Her only

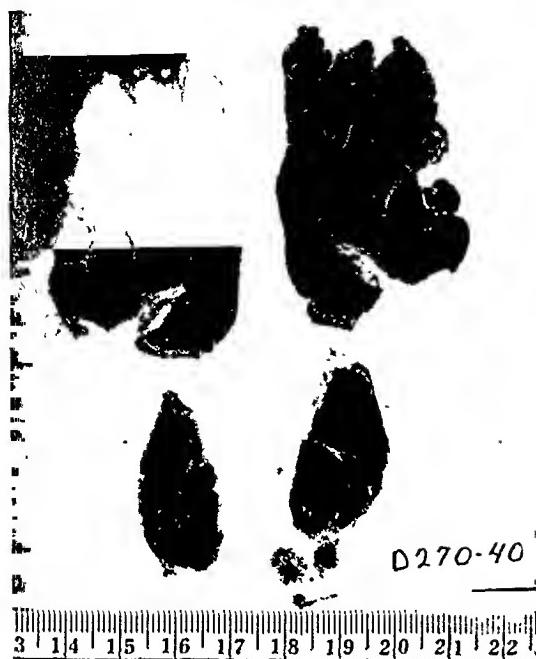


FIG. 1. Photograph of cut surface of both lobes, isthmus and pyramidal lobe showing lobular appearance and diffuse involvement.

complaints at present are of occasional tiredness and mild aching in the extremities.

\* There was a diffuse enlargement of both lobes, the isthmus and pyramidal lobe. (Fig. 1.) The right lobe measured 5 by 2.5 by 1.5 cm. and the left lobe was 5.5 by 3 cm. The cut surface did not resemble thyroid tissue; except for its color it simulated a lymph-node rather than thyroid. It was yellow-grey, bloodless, dry, very finely adenomatous in appearance, very firm but not hard. No parathyroids were noted.

Microscopically, (Figs. 2 and 3) the tissue presented an unusual picture. The normal acinar structure was obliterated by large numbers of lymphocytes which were widely scattered in the interstitial tissue. In places they coalesced in masses which replaced the alveoli. Some of these areas represented typical lymphoid follicles. There was a proliferation of interstitial connective tissue, in most instances in the form of fine, collagenous fibers which, in a few areas, were condensed into coarse bands. The thyroid alveoli were seen with difficulty not

only because of the changes just described, but also because of the greatly diminished amount of colloid. In some areas, degenerating alveoli with their coalesced nuclei simulated giant cells. Lymph channels or spaces containing lymphocytes were seen. There was no evidence of malignancy.

*Discussion.* The short duration of symptoms is of interest in this patient. In 104 cases of so-called chronic thyroiditis reviewed by Graham,<sup>6</sup> the average duration of twenty-four cases of Hashimoto's disease was 1.2 years.

Struma lymphomatosa occurs chiefly in women near or following the menopause. In Graham's series, 95.8 per cent occurred in women and the average age was 52.4 years. Judd<sup>7</sup> and Kearns<sup>8</sup> have each reported a case in a male.

The etiology of this disease is not definitely known. Most authorities<sup>9-12</sup> consider the condition a form of chronic thyroiditis. It is noteworthy that a transient thyroid enlargement was felt by the patient eight months before the symptom became established. The question arises as to whether or not this condition may have been a subacute inflammatory phenomenon, the forerunner of her present illness. Means<sup>3</sup> is of the opinion that the etiology of both Hashimoto's and Riedel's disease is different, although unknown, than that of acute thyroiditis.

The possibility of degenerative changes on a physiologic evolutionary basis has been suggested by Jaffe.<sup>13</sup> This theory attempts to account for the occurrence of the disease mainly in women past the menopause. The concept of Eisen<sup>14</sup> and Ewing<sup>15</sup> that struma lymphomatosa is the early stage and Riedel's struma the late stage of the same disease is difficult to accept for the following reasons: First, in Hashimoto's disease where there is minimal fibrosis and the pathology is entirely intracapsular, the duration of symptoms is longer than in Riedel's struma in which fibrosis is advanced and extends through the capsule to the surrounding structures (1.2 years compared to 7.3 months in

\* Pathologic examination reported by Dr. John Tragerman.

Graham's series). Second, the high incidence of Hashimoto's disease in women in contrast to the occurrence of Riedel's

was changed at this time to carcinoma. Hence, a total thyroidectomy was performed. Not until the microscopic sections

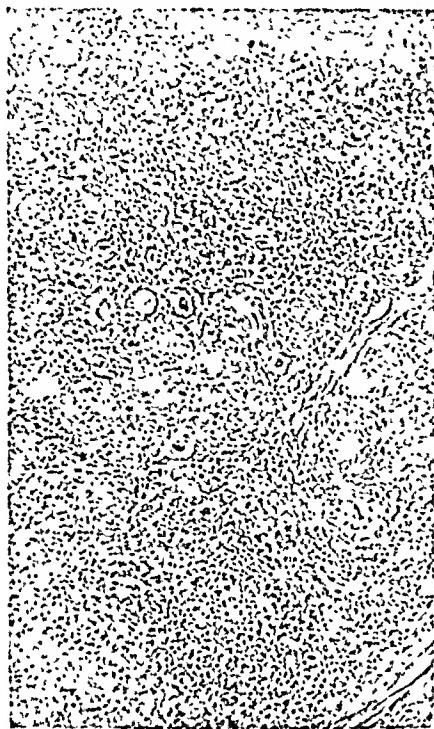


FIG. 2. Low power photomicrograph of section taken from thyroid. Note lymphocytic infiltration with tendency to germinal follicle formation, degenerated and atrophic alveoli, decrease in colloid and fibrous trabeculae characteristic of Hashimoto's disease.

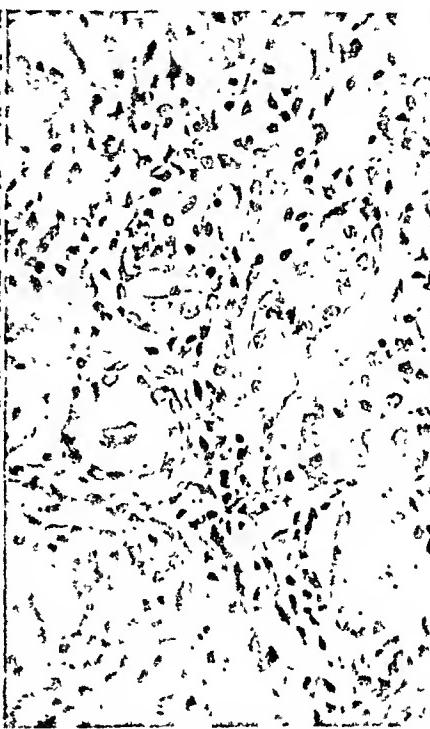


FIG. 3. High power photomicrograph of section of thyroid showing in detail the degenerated alveolar epithelium and almost complete lack of colloid.

were completed was the true diagnosis known.

The disease pursues a progressive course and ultimately the patient suffers from hypothyroidism or even myxedema<sup>17,18</sup> regardless of the method of treatment. Pressure symptoms including dyspnea and dysphagia may appear before this state is reached.

Because of its lymphoid nature, Hashimoto's disease is radiosensitive. However, because of the uncertain clinical differentiation from carcinoma, it would be unwise to employ such therapy merely upon suspicion. Operation is the safest procedure, with relief of compression the chief aim. If the findings here suggest a condition other than typical hyperplastic or adenomatous goiter, a biopsy with rapid frozen section is indicated. Should the microscopic picture be that of struma lymphomatosa with malignancy excluded,

struma in both men and women seems to refute this belief.

It is our opinion that the presence of syphilis in this patient was entirely coincidental. Vogel<sup>16</sup> says that syphilis of the thyroid may show diffuse sclerosis or a gumma, and that the latter is difficult to differentiate from a tumor. In this instance, however, the gross and microscopic findings were distinctive of struma lymphomatosa.

The preoperative diagnosis in our case was adenomatous goiter. At operation it was noted that, in spite of the enlarged, firm gland, there was no unusual adherence to surrounding structures. Notwithstanding this puzzling feature which is typical of Hashimoto's disease, the clinical diagnosis

a generous subtotal thyroidectomy is the best treatment. This procedure will accomplish the purpose of relief of compression and will minimize the danger of injury to the parathyroids and recurrent laryngeal nerves associated with total resection. Radiation may be employed later if necessary.

#### SUMMARY

Hashimoto's disease is characterized by a diffuse, resilient enlargement of the thyroid gland. The pathological condition is confined within the capsule and there is little or no adherence to surrounding structures. The fibrous trabeculae produce a lobulated appearance and may account for a preoperative impression of adenomatous goiter. Microscopically, the distinguishing features consist of degeneration and disappearance of the alveoli due to marked lymphocytic infiltration. Where masses of lymphocytes have coalesced, germinal follicles may be seen. Moderate fibrosis is present, tending to form bands. The alveoli are atrophic and compressed. Atrophic, degenerated alveoli with their coalesced nuclei may easily be confused with giant cells.

#### CONCLUSIONS

1. The etiology of Hashimoto's disease is not definitely known.
2. Evidence indicates that struma lymphomatosa is not the early stage of Riedel's struma.
3. If findings at operation suggest a condition other than typical hyperplastic

or adenomatous goiter, a rapid frozen section biopsy is indicated.

4. With malignancy excluded, the most logical form of therapy is a generous subtotal resection.

5. Regardless of the method of treatment, gradations from mild hypothyroidism to true myxedema ultimately result in the majority of these patients.

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# THE VALUE OF VARYING THE POSITION OF THE McBURNEY INCISION\*

HOWARD D. COGSWELL, M.D.

Surgeon, Whiting Clinic

WHITING, INDIANA

THE muscle splitting incision introduced by McBurney in 1893, and now bearing his name, has obtained wide popularity and is the most commonly used incision in the performance of an appendectomy. It is described as an incision in which the skin is split obliquely and parallel with Poupart's ligament, 4 cm. mesial to the right anteriosuperior spine. It should be crossed just above its middle by a line connecting the umbilicus and the anteriosuperior spine. Thus, the classical McBurney incision is always made in the same area, fixed landmarks being used for its localization. Considering the variable positions assumed by both the cecum and the appendix, it is obvious that the classical McBurney incision is frequently above or below the site to be operated upon. Christopher<sup>1</sup> has suggested modifying the location of the McBurney incision by placing it where it will best serve to expose the appendix to view, and Royster<sup>2</sup> has said that the incision "may be placed in an oblique direction anywhere in the right iliac area." That these suggestions are not being universally or even commonly followed is attested by the observation that most appendectomy scars are found to be centered over McBurney's point and by seeing experienced surgeons routinely make their incisions in this location.

A fact that does not seem to be generally appreciated is that there is a great variation in the exact spot of maximum tenderness in the right lower quadrant in cases of appendicitis. As Royster states, "In determining the sensitiveness to pressure the clinician is more interested in its diagnostic aspects than in its definite anatomical

position." This point of maximum tenderness in cases of appendicitis corresponds to the base of the appendix, as it is from here that the afferent nerves from the appendix transmit sensation. Prudent palpation after the diagnosis of appendicitis has been made will reveal one point in the right lower quadrant where the tenderness is maximal and where minimal pressure is required to evoke a response from the patient. The incision should be centered over this point since it directly overlies the appendix and direct access is afforded for an appendectomy.

Objection to McBurney's incision has been raised on the ground that ample room is not afforded for a safe appendectomy. Saint<sup>3</sup> has recently advocated a muscle cutting incision in place of the McBurney incision, stating that "a surprising amount of room is provided for surgical manipulations in contrast to that available through the muscle-splitting incision." The use of this incision apparently has been satisfactory in his hands but may be objected to, on the ground that since the internal oblique and transversalis muscles and the transversalis fascia are cut, the wound would be much more liable to herniation. If more attention were given to the site of maximum tenderness, the modified McBurney incision would be placed over the viscera to be operated upon, thereby making the cutting of muscles unnecessary.

In instances in which room is needed, the wound may be enlarged, either upward or downward, by cutting along the junction of the internal and external oblique aponeuroses with the sheath of the rectus abdominis muscle and turning the flap

\* From The Whiting Clinic, Whiting, Indiana.

lateralward. The peritoneum is divided in the same direction as the skin incision. A second maneuver which facilitates removal of appendices of the undescended type, in which the tip lies higher than the base, is the "double McBurney" incision. Dr. W. D. Gatch, although possibly not the originator of this modification, was the one to impress this writer with its usefulness. After an incision has been made over the point of maximum tenderness, and the appendix is found to be inaccessible, the skin incision is extended upward to the area overlying the tip of the appendix. Here the external and internal oblique muscles are split in the direction of their fibers and the peritoneum is incised obliquely. It will be found that the appendix may be visualized and safely removed by working through both the upper and lower incisions, although removal had appeared impossible through the lower opening alone.

Every active surgeon has had the experience of opening the abdomen believing an appendicitis to be present and finding other conditions responsible for the symptoms. If the incision has been made over the point of maximum tenderness, the diseased viscous is exposed whether it be a fallopian tube, Meckle's diverticulum, ruptured cystic ovary or other lesion. When adnexal

disease is unexpectedly found, the McBurney incision should be closed and the operation carried out through a midline incision, since adnexal disease is often bilateral. It is hazardous to attempt to remove the adnexa of the left side through a right-sided incision.

Care should be exercised when making a low incision not to injure the internal inguinal ring or the ilio-inguinal nerve. These can easily be avoided, however, and should cause no concern if caution is used.

#### SUMMARY

In the performance of an appendectomy the muscle splitting incision should be centered over the point of maximum tenderness. This point corresponds to the base of the appendix and an incision at this point gives better exposure than the classical McBurney incision.

I wish to express my appreciation to Dr. John Alexander, of Ann Arbor, Michigan, for his suggestions in the preparation of this paper.

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# LOCATING ACUTE APPENDICITIS PRIOR TO SURGERY\*

KARL E. VOLDENG, M.D.

WELLINGTON, KANSAS

THE following discussion is designed to stimulate consideration of a point which has been emphasized by many surgeons previously, however, it is still not receiving the attention it deserves.

When Reginald Fitz,<sup>1</sup> in 1886, used the term "appendicitis," for the first time his account of this condition inaugurated a crusade against a serious and frequent threat to life. Countless contributions since that time have refined the diagnostic and surgical principles involved, with a resulting situation which permits a very satisfactory management for acute appendicitis.

There continues to exist a mortality from acute appendicitis which prompts the appearance of further helpful contributions in the literature. To lessen this mortality, the surgeon has as his responsibility a constant striving toward a technically perfect appendectomy. At the present time the great majority of surgeons terminate their diagnostic trend of thought as soon as the diagnosis of acute appendicitis is made. As a rule little effort is made to visualize the exact situation of the inflamed structure.

If the surgeon could, prior to surgery outline the relative situation of the appendix, it would assist his surgical technic in two particular points: (1) An incision would be chosen to give better exposure and a more direct approach to the infected area. (2) Less intra-abdominal manipulation and exploration would be necessary, thus avoiding all possible general contamination.

For the past year the author has carried out the following procedure: As soon as a diagnosis of acute appendicitis is made, the patient is prepared for surgery. The pre-operative orders are instituted which usu-

ally consist of morphine, atropine and one of the barbiturates. A sufficient time remains before the patient is brought to the operating room for these medications to have a full effect. Just before the patient is taken to the operating room an attempt is made by point pressure to localize the site of the appendix. The abdomen in this final examination differs materially from the condition which existed prior to any medication. Any pre-existing rigidity has been distinctly lessened or abolished. The patient is much more mentally at ease, physically relaxed, and secondary areas of tenderness throughout the abdomen have largely disappeared. In fact, tenderness is usually found to exist only directly over the appendix. At times an edematous, indurated appendix can actually be palpated through a soft, thin, abdominal wall.

Charles McBurney,<sup>2</sup> in 1889, overstressed the importance of the so-called McBurney's point. According to his own words: ". . . the point of greatest tenderness is, in the average adult, almost exactly two inches from the anterior iliac spine, on a line drawn from this process through the umbilicus. . . . This point indicates the situation of the base of the appendix, where it arises from the cecum, . . . "

Anatomists, radiologists and surgeons have repeatedly proved that the appendix has a wide range of position, in fact, the base of the appendix is only rarely exactly at McBurney's (or more properly, McArthur's) point. Barclay<sup>3</sup> in careful radiological studies found only seven out of thirty to have the junction of appendix and cecum fall anyway near McBurney's point. This variation is due entirely to normal anatomical discrepancies, since numerous investigators such as Collins<sup>4</sup> have shown

\* From the Hatcher Clinic, Wellington, Kansas.

that approximately 70 per cent of all appendices are free and must be considered to be in normal position.

In actual clinical practice, following the above suggested technic, the point of maximum tenderness will in the great majority of cases distinctly locate the inflamed appendix. The latterly placed tenderness of a retrocecal appendicitis is well recognized. An acutely infected appendix situated well over the pelvic brim may show a more definite point tenderness by rectal examination.

As a supplement to such a careful finger point localization of the tender point, the clinical history may offer valuable help. The retrocecal appendix elicits a rather unusual history which has been well analyzed by Collins.<sup>5</sup> A pelvic appendicitis also may present a bizarre clinical picture.<sup>6</sup> When the appendix is adjacent to a kidney, the ureter, urinary bladder or sigmoid, the clinical story may give a clue. In every case, a careful bedside story must be obtained and this picture fitted in with the findings of point tenderness, for a complete final effort to locate the appendix definitely.

When the appendix is believed to reside at or near McBurney's point, most surgeons prefer the muscle splitting or "gridiron" incision. This entrance through the abdominal wall is designed to fulfill all requirements except exposure. If this muscle splitting incision can be placed more accurately over the appendix, the surgeon will be materially helped by a mere quarter inch of advantage. The lower right abdominal quadrant will allow a remarkably wide variation in the location for a muscle splitting incision.

If the incision is placed laterally, it will be best patterned after the technic of the late Rutherford Morison which has recently been well described by Saint.<sup>7</sup> Other, more radical incisions have been developed for the safer approach to a true retrocecal appendix (Willy Meyer<sup>8</sup>). For a more medially situated appendix the Battle incision or perirectus route may be desired.

When the infected process is in a pelvic location, a right rectus or right perimedial incision may be desired.

The real value of a direct approach to the inflamed appendix is realized by the surgeon when he begins his exploration for the diseased structure. With a preoperative conception of where the appendix is situated and with an incision that directly overlies this area, the surgeon greatly increases his possibility of removing a badly infected, oozing appendix with the least possible contamination of surrounding peritoneal structures. Any attempt by nature to wall off the infectious process will receive a minimal disturbance. Drainage, if necessary, will be simplified. In every way the surgeon will improve technically and practically the act of appendectomy.

#### SUMMARY

An effort is made to encourage the general surgeon to evaluate the history and physical findings more carefully of each patient going to surgery with an acute appendicitis. It is the author's belief that a more accurate localization of the diseased organ can be made through physical findings plus clinical history which will distinctly assist in the procedure of appendectomy.

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# COSTO-ILIAC BLOCK IN BALANCED ANESTHESIA FOR APPENDECTOMY IN THE SMALL HOSPITAL

CALEB H. SMITH, M.D.

Surgeon, Bradford Hospital

BRADFORD, PENNSYLVANIA

**C**OSTO-ILIAC block can be a valuable part of balanced anesthesia for appendectomy in the small hospital. When inhalation anesthesia is undesirable, as in respiratory infections, it is particularly useful. In small hospitals reliable spinal anesthesia may not be available because a physician anesthetist is usually not in attendance and many surgeons in such institutions are not experienced in spinal anesthesia.

When inhalation anesthesia is to be avoided and the cough reflex retained, costo-iliac block will permit a painless laparotomy through a McBurney incision with excellent muscular relaxation. When the appendix is readily accessible and the surgeon gentle, it may be possible to remove the appendix without further anesthesia. If this procedure is painful, a light cyclopropane anesthesia may be used while the appendix is actually removed. This gas anesthesia is discontinued before closure of the peritoneum is begun. The patient is awake and coughing before the wound is closed. Coughing is particularly active when there is an appreciable amount of bronchial secretion. During coughing it is interesting to note how efficiently contraction of the oblique muscles tends to close the incision.

After any surgical procedure there is danger of pulmonary complications. Such complications usually begin with obstruction of a bronchus with secretions and subsequent atelectasis. Preservation of the cough reflex is the simplest and most efficient precaution against such accidents.

Costo-iliac block permits an early return of the cough reflex in the usual appendectomy. In cases in which no particular

contraindication to inhalation anesthesia exists, a light cyclopropane anesthesia is induced. The patient is draped in the usual manner. A costo-iliac block is then done. Appendectomy can be carried out with little inhalation anesthesia. The excellent muscular relaxation obtained permits easy access to the pelvis when necessary.

Very often the patient is awake and coughing before he is removed from the operating table. Usually he is awake when he reaches his room. By this procedure coughing begins hours before it does after an ordinary inhalation anesthesia and the patient is protected against pulmonary complications. Furthermore the patient and his family are usually pleased with his rapid recovery from his inhalation anesthesia.

When costo-iliac block is used 2 or 3 gr. of sodium phenobarbital are given hypodermically preoperatively as a protection against a reaction to procaine hydrochloride. Such medication must not be given in large doses for it tends to suppress the cough reflex in itself.

## TECHNIC OF COSTO-ILIAC BLOCK

Costo-iliac block was described by Labat.<sup>1</sup> A skin wheal is raised about two finger breadths (4 em.) posterior to and above the anterior superior spine. A second wheal is raised below the costal margin at about the level of the tip of the eleventh rib. The needle is passed through each of these wheals in succession and a 0.5 per cent solution of procaine hydrochloride containing adrenalin hydrochloride 1:100,000 is distributed fan-wise within the muscle layer as well as subcutaneously between the costal margin and the iliac

crest. The injections are always made at right angles to the surface of the skin. The block can be executed in a few minutes.

#### SUMMARY

Costo-iliac block is a valuable procedure in small hospitals where spinal anesthesia is not available. It may permit the cough

reflex to be retained or at least to return soon after the operation thereby affording some protection against postoperative pulmonary complications.

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IN the acute condition of inversion of the uterus and where there is no evidence of an infected organ, indication is that of preservation of the uterus by returning the organ to its normal position through reduction of the inversion.

The brief excerpts in this issue have been taken from "Vaginal Hysterectomy" by James William Kennedy and Archibald Donald Campbell (F. A. Davis Company).

# THE SCALENUS ANTICUS SYNDROME

## FAULTY DIAGNOSIS IN PRESENCE OF HORNER'S SYNDROME—A MODIFIED TECHNIC OF INFILTRATION

BERNARD JUDOVICH, M.D.

AND

WILLIAM BATES, M.D.

Chief of Neuralgia Clinic, Department of Neuro-  
psychiatry, Philadelphia General Hospital

Professor of Surgery, Graduate School of Medicine,  
University of Pennsylvania

PHILADELPHIA, PENNSYLVANIA

**D**IAGNOSTIC injection of the scalenus anticus muscle with procaine is a valuable procedure in eliminating causes of brachial plexus pain. In attempting to relieve pain in the upper extremity by procainization of the scalenus anticus muscle, observers state that in numerous patients they had obtained a Horner's syndrome. Although it is true that through the scalenus mechanism there may be irritation of the sympathetics, it is a secondary effect; and infiltration of the muscle with procaine which results in a Horner's syndrome with relief of pain should not be considered evidence that the muscle is at fault. Sympathetic anesthesia appears to be an undesirable effect. Blocking of the cervical sympathetic chain is capable of relieving pain other than that which is scalenus anticus in origin. Another important fact is that an infiltration resulting in a Horner's syndrome produces an effect which is not duplicated by section of the muscle.

To obtain a proper evaluation of this syndrome, we believe that the infiltration should be limited to the boundaries of the muscle, and that when a Horner's syndrome is obtained, operation should be deferred until successful muscle infiltration without the sympathetic effect has been obtained. Also, any form of peripheral anesthesia following the injection would indicate that the test should be repeated.

In three consecutive cases, failures followed cutting of the anterior scalenus muscle after complete relief was obtained by infiltration with procaine solution. All three had developed a Horner's syndrome

with the injections. One of these patients had a bilateral section. Following infiltration, she had developed a sympathetic anesthesia on each side.

In a patient who was injected twice with procaine, a Horner's syndrome developed on one occasion, and none on the other, complete relief being obtained in both instances. Section of the muscle was followed by cessation of pain.

In another case, the muscle was infiltrated with little relief of pain. After a fifteen minute waiting period, we deliberately introduced a longer needle and produced a Horner's syndrome with immediate disappearance of all pain. Needless to say, this muscle was not cut.

Modification of our technic and disregarding relief of pain in the presence of a Horner's syndrome gave us highly satisfactory results. Patients in seven consecutive cases were completely relieved by muscle section.

We believe that errors may be avoided by not infiltrating too deeply and by attempting to make certain that the injection is confined to the muscle. To this end we have devised the following technic:

### HYPONEEDLE TECHNIC OF SCALENUS ANTICUS INJECTION

The patient's chin is turned to the non-painful side and the head slightly retracted. This brings the muscles in this area into greater prominence. The lateral border of the tip of the left, middle finger is placed against the outer border of the sternocleidomastoid muscle just above its clavicular attachment, with the forefinger

spaced about three-fourths of an inch away. At the same time the clavicular head of the sternomastoid muscle is pushed medially.

Pressure is made downward and behind the clavicle so that the two fingers straddle the first rib at the insertion of the scalenus muscle. The first rib can be further palpated by the index finger of the right hand. From this point upward the course of the muscle can be followed. Maneuvering the head with the free hand alternately flexing and extending the muscles will help while palpating.

When the insertion of the muscle is well localized, the two fingers "crawl" upward along its belly to a point about one and one-half inches above the clavicle. The muscle is thus confined to the space between the two fingers and with inward pressure is held taut, so that the muscle bellies outward between the two fingers. An ordinary one-half inch hypodermic needle is inserted full length into the muscle and the procaine solution injected.

#### SUMMARY

In patients with brachial plexus pain, diagnostic infiltration of the scalenus anticus muscle with procaine must be interpreted very carefully. If, following injection, relief of pain is accompanied by a Horner's syndrome, the entire result should be ignored, and surgical approach should be postponed until a successful muscle infiltration without the sympathetic anesthesia has been obtained. Anesthesia of the cervical sympathetics will stop pain which is not scalenus anticus in origin. Also, it is an effect not duplicated by section of the muscle. In our experience, surgical failures have predominated when these facts have been ignored. We have introduced a hypo-needle technic, in which the scalenus anticus muscle may be successfully injected with little likelihood of producing a Horner's syndrome.

Following these modifications of clinical interpretation and technic, our surgical efforts have been rewarded with gratifying results.



## KIDNEY ILLUSTRATIONS

**K**NOWLEDGE regarding the kidneys is part of the fund of information which every doctor possesses regarding the body mechanism. That profound changes take place when the vital functions of these important organs are impaired is also well known. Such damage results in alterations of urinary secretion, water balance and osmotic relations between blood and tissues. These changes are reflected clinically in generalized edema, uremia and many other symptoms which are associated with the conditions commonly referred to as nephritis and nephrosis.

The contributions of medical artists who can furnish a clear representation of microscopic anatomy are always held in high esteem. The value of such work is further enhanced when, from a study of the structural details and the functional mechanisms involved, the artist can paint a clear picture of both anatomy and physiology.

The following illustrations are examples of such fine work and are unique in their field. The true anatomie picture of the kidney is given as well as a reconstruction of the nephron in both health and disease. Likewise, the informative labeling has been done with painstaking care.

The author of the set of color illustrations offered in this issue is Lieutenant Leon Schlossberg, formerly at the Johns Hopkins Hospital and now in active service with the U. S. Navy. Winthrop Chemical Company, Inc., was kind enough to supply these handsome reproductions for the benefit of our subscribers. We are of the opinion that our readers will welcome these valuable drawings of the renal organs.

T. S. W.

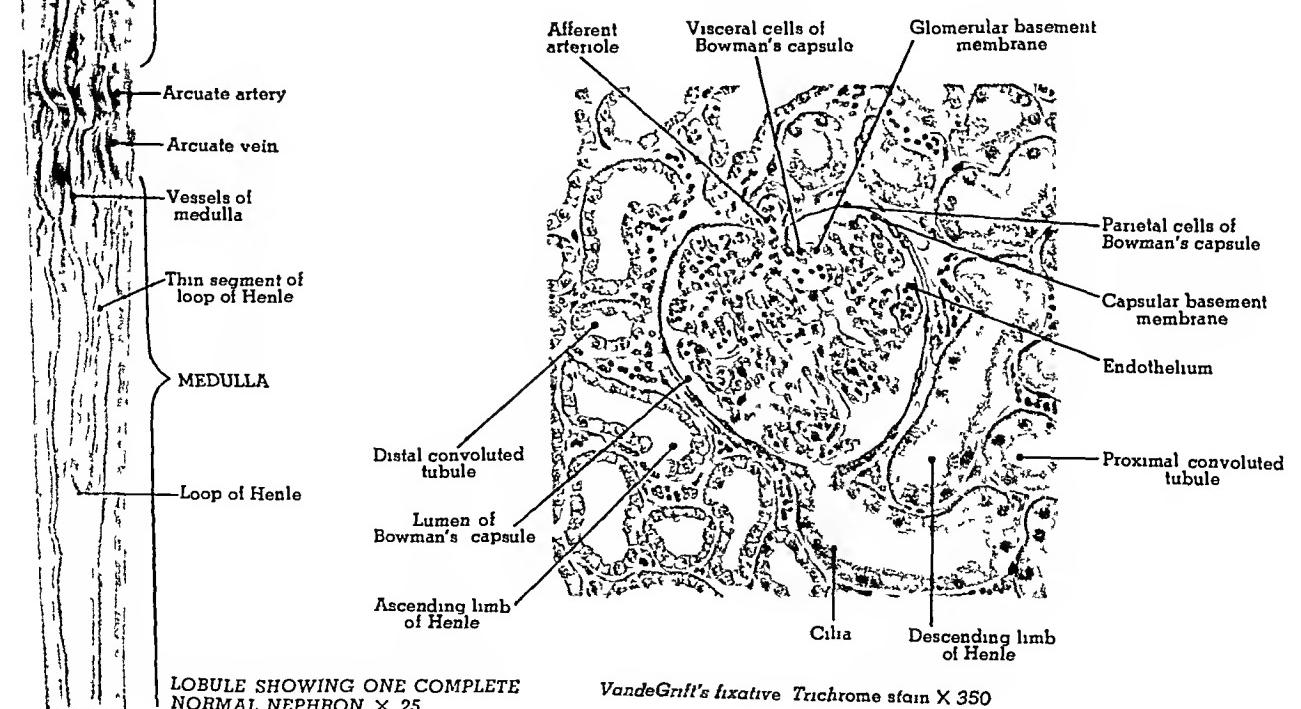
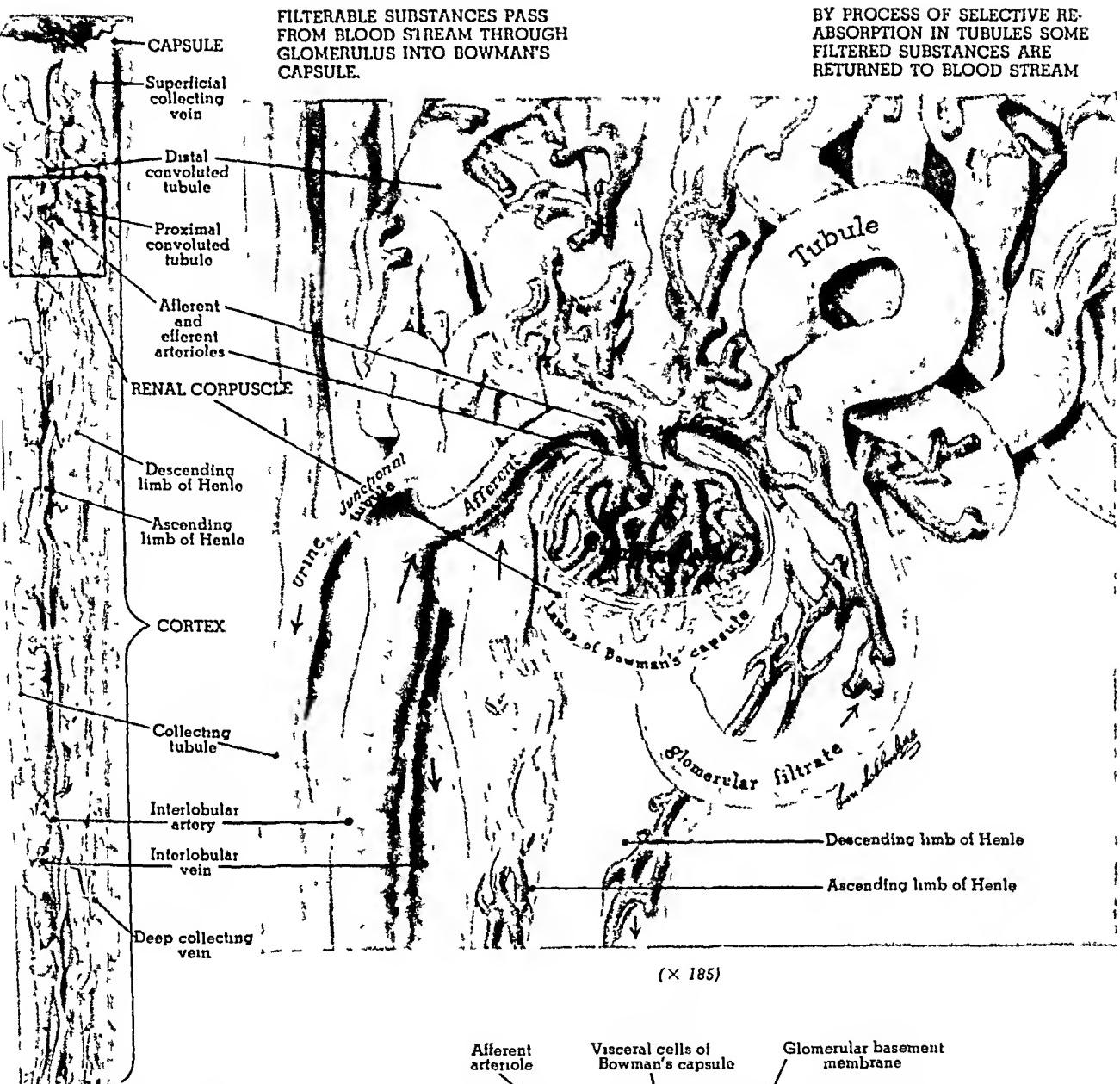
## NEPHRON OF NORMAL KIDNEY

CUSHNY'S concept that urine is secreted by a process of glomerular filtration and selective tubular reabsorption is widely accepted. According to his views the composition of the fluid passing from the capillaries of a glomerulus into the lumen of Bowman's capsule (the expanded extremity of the renal tubule) is virtually identical with that of the plasma of the blood with the exception that the glomerular filtrate does not contain the colloids, i.e., the proteins and fats. As the glomerular filtrate flows through the tubules it is transformed into urine by selective reabsorption of certain constituents into the blood stream. Water is normally reabsorbed to the extent of 98.5 percent. Substances such as glucose, amino-acids, chlorides, sodium, potassium and calcium are reabsorbed to a considerable degree, so that they are absent from normal urine or present only in low concentration. On the other hand, creatinine, urea, uric acid, phosphates and sulfates are reabsorbed in small amounts or not at all. Hence, relatively large quantities of these "waste products" appear in the urine.

Cushny does not attribute to the tubules any additional function. However, more recent studies have furnished evidence that the tubular epithelium may also actively excrete some urinary constituents, e.g., urea and creatinine, and synthesize others, such as ammonia and hippuric acid.

The work done by the kidneys is of great importance in physiologic economy. Through the secretion of urine these organs are intimately concerned with the water metabolism of the body and also aid in maintaining the hydrogen ion concentration of the blood as well as the equilibrium of factors which regulate osmotic relations between blood and tissues.



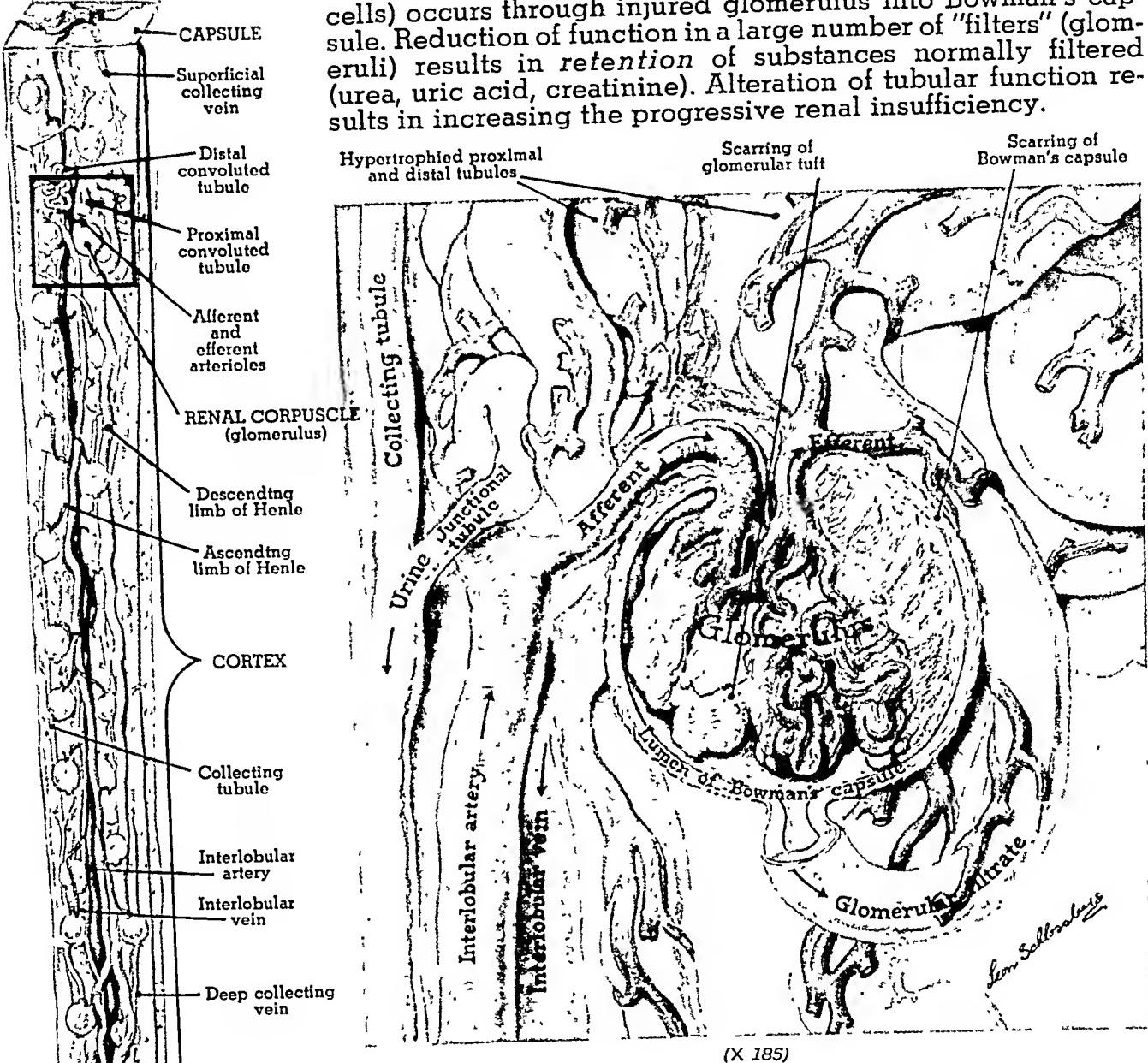


## NEPHRON IN CHRONIC GLOMERULAR NEPHRITIS

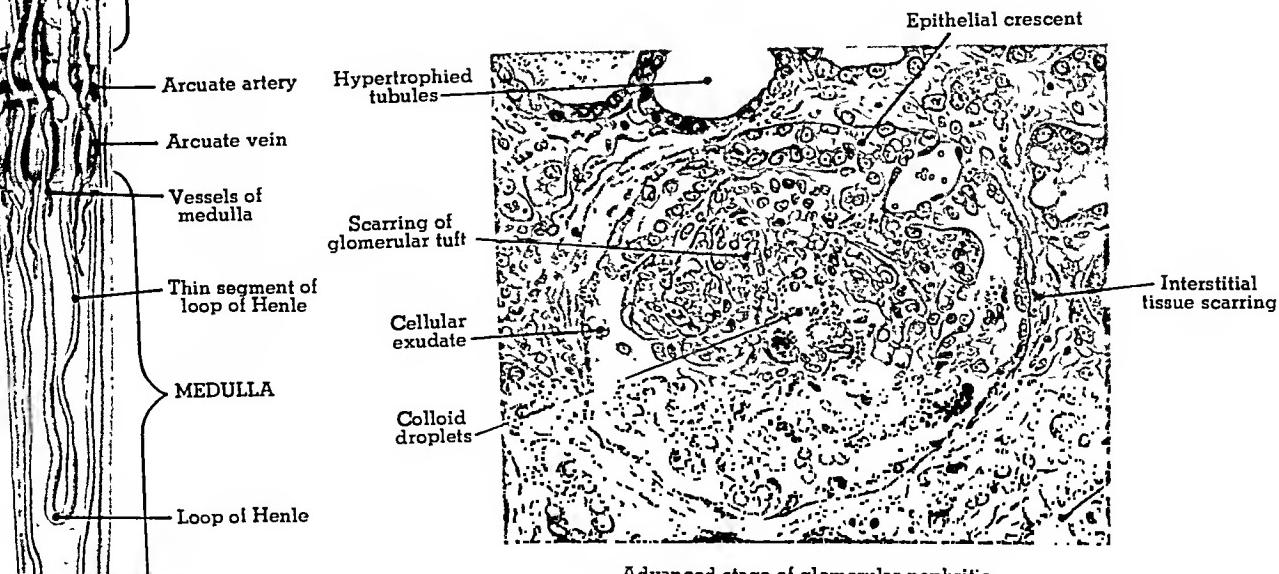
THE pathologic lesions which occur in chronic glomerular nephritis bring about a considerable alteration in the physiologic function of the kidneys. In this disease, as a result of the injury sustained by the glomeruli, there is a leakage of normally nonfiltrable substances (proteins and cells) which appear in the urine in variable amounts, depending upon the degree of damage produced. Hence, albumin and various types of casts are commonly found in such cases. When the total available filtering surface is reduced there develop the signs of renal insufficiency. Excretion of the nonprotein nitrogenous products (urea, uric acid, creatinine) being interfered with, the capacity of the kidneys to excrete water within the normal time after its ingestion is lessened. Edema may develop which becomes more severe with the steady loss into the urine of serum proteins. Moreover, sooner or later the tubules become involved in the progressive degenerative disease. When this takes place to any considerable extent the function of the kidneys, such as their ability to concentrate water, is further impaired.



Leakage of normally nonfiltrable substances (proteins and cells) occurs through injured glomerulus into Bowman's capsule. Reduction of function in a large number of "filters" (glomeruli) results in retention of substances normally filtered (urea, uric acid, creatinine). Alteration of tubular function results in increasing the progressive renal insufficiency.



(X 185)



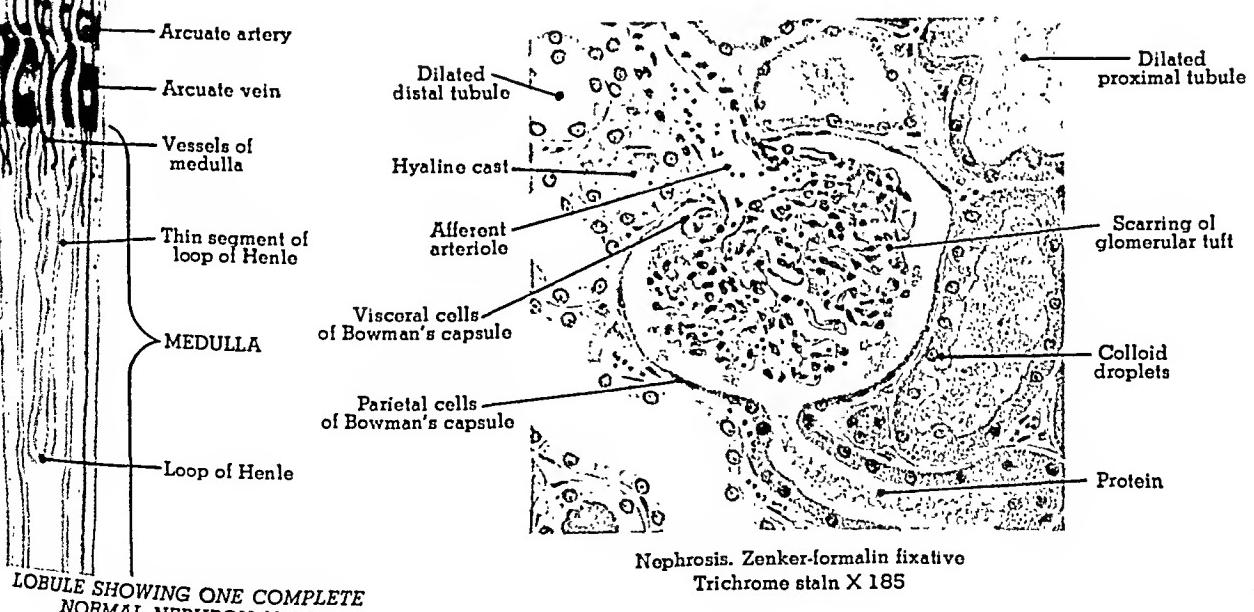
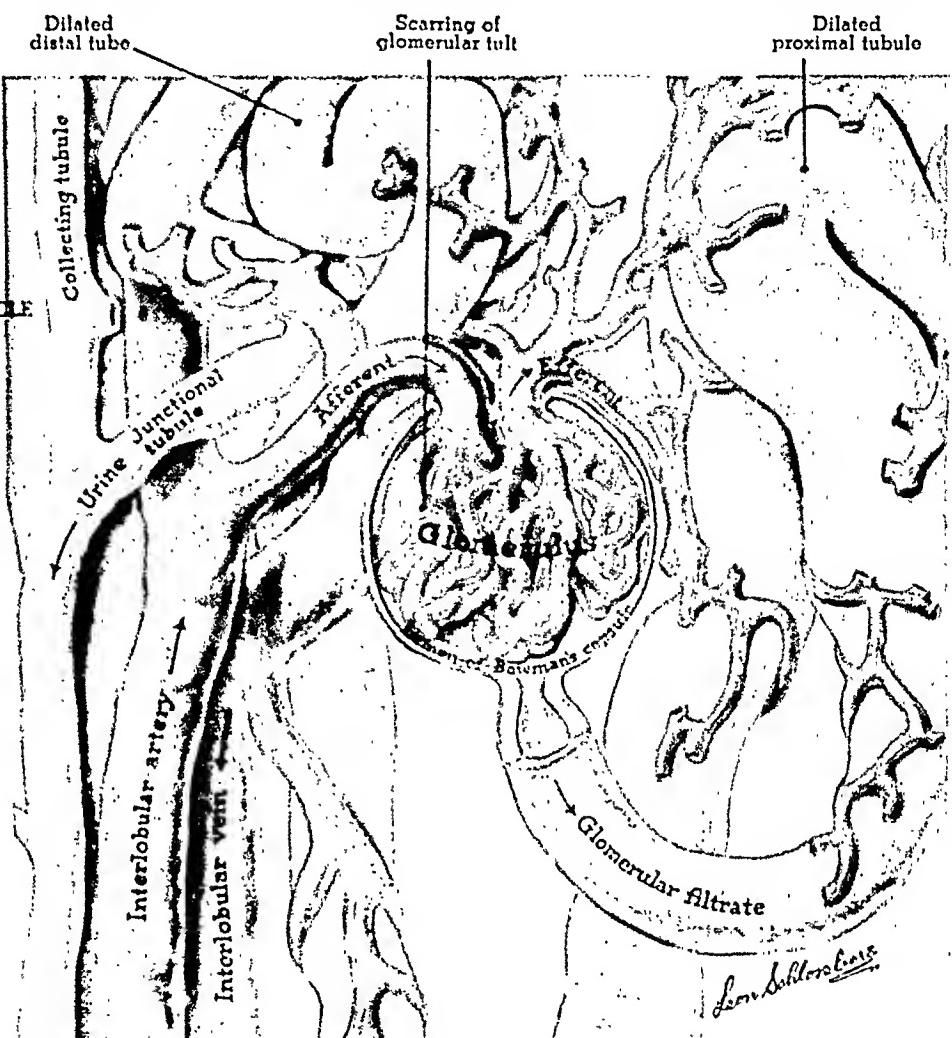
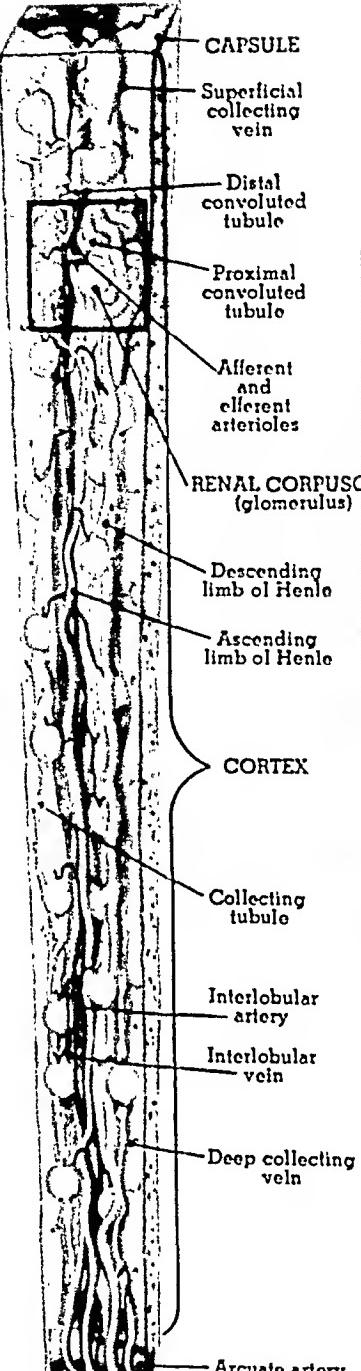
Advanced stage of glomerular nephritis.  
Zenker-formalin fixative. Trichrome stain X 250

## NEPHRON IN NEPHROSIS

NEPHROSIS is characterized pathologically by extensive degeneration of the renal tubules. Visible glomerular or vascular lesions are generally not a prominent feature but there is little doubt that profound changes of a functional nature occur in the glomeruli. As a result there is leakage of proteins, which are normally nonfiltrable, through the altered glomerular tufts. Large quantities of the serum proteins are excreted in the urine; consequently there is a deficit in the blood plasma. As a result plasma osmotic pressure is lowered, and fluid and salt are retained in the tissue spaces. These changes are expressed clinically in generalized edema. Symptoms of renal insufficiency and cardiac hypertrophy with hypertension do not develop in typical cases of nephrosis. The outstanding findings are the serious loss of blood albumin, generalized dropsy, decreased urinary output and albuminuria accompanied from time to time by heavy showers of tubular casts.



Leakage of proteins, normally nonfiltrable, occurs because of functional or ultramicroscopic alterations of glomerulus. With excessive loss of protein a deficit in the blood plasma occurs and generalized edema results. Degenerative changes in tubules are extensive but renal insufficiency is uncommon.



LOBULE SHOWING ONE COMPLETE NORMAL NEPHRON X 25

## ALTERED MECHANISM IN DROPSY

WHEN glomerular and tubular functions become impaired, alterations in the mechanism of urinary secretion occur. Depending upon which of these two functions is mainly affected and the degree of involvement, there develop systemic changes that are discernible clinically and by laboratory tests. Thus there may be retention of water with resulting generalized edema, or accumulation of waste products with subsequent azotemia (uremia).

Three distinct varieties of edema are differentiated. Nephritic edema is characterized by an increase in the permeability of the capillaries so that protein passes through; the protein content of the edema fluid is high. It occurs in glomerulonephritis and can be produced experimentally by damage of the capillaries with such substances as uranium or arsenic.

Nephrotic edema is due to decreased colloid osmotic pressure of the plasma proteins; the edema fluid has a very low protein content. It is encountered in chronic nephrosis, the nephrotic type of glomerulonephritis, the amyloid kidney and hunger edema.

In cardiac edema there is an increase in the capillary pressure; the protein content of the edema fluid is variable.

The extent of each type of edema is materially influenced by various secondary factors, such as the presence or absence of renal insufficiency and the quantity of salt and water ingested.



# Case Reports

## ENTEROCYSTOMAS

### REPORT OF A PATIENT WITH DUPLICATION OF THE STOMACH

FRANCIS P. FERRARO, M.D.  
On Surgical Staff, St. Francis Hospital  
PITTSBURGH, PENNSYLVANIA

ENTEROCYSTOMAS, also known as enterogenous or enteric cysts, of true developmental origin are quite rare and may occur anywhere in the alimentary tract from the base of the tongue to the rectum. An idea as to the rarity is given by Mayer<sup>1</sup> who states: "In the local hospital records of over 80,000 patients no enteric cysts have been recorded." The most common site of occurrence is the region of the ileum and cecum, Hamilton,<sup>2</sup> Slesinger,<sup>3</sup> Haggard,<sup>4</sup> Kettell,<sup>5</sup> Sherwin,<sup>6</sup> and Pachman<sup>7</sup> all reporting cases in this region. In addition, Kettell<sup>5</sup> reviews eighty-eight cases from the literature of which seventy-one were connected with the small intestine and seventeen with the colon. Pachman<sup>7</sup> in his paper states that up until 1939 only eight cases of duodenal enterocystomas had been reported. Mayer's<sup>1</sup> case is one involving the transverse mesocolon while Ladd and Gross,<sup>8</sup> in the most varied series reported, mention eighteen cases situated as follows: base of tongue, one; esophagus, three; stomach, one; duodenum, one; jejunum, two; ileum, seven; cecum, one; sigmoid, one; and rectum, one. Mc Lanahan and Stone<sup>9</sup> report two cases involving the rectum.

Although it is mentioned<sup>1,6,8,9</sup> that these cysts have been described as occurring along every portion of the alimentary tract, the stomach case of Ladd and Gross<sup>8</sup> is the only one we have been able to locate. The purpose of this paper is to report a case of

enterocystoma of the stomach which had several unusual complications.

#### CASE REPORT

J. R. S., age six months, was admitted to the hospital\* March 3, 1941, because of a "draining hole on the belly." Her mother stated that shortly after birth she had noted a mass in the infant's "belly" and as it had gradually become larger she took the infant to a physician who, when the baby was six weeks old, incised the mass. Since then the operative area had never healed and had continuously drained a watery fluid. The patient also had a quite persistent diarrhea which had been present for several weeks and at times would vomit her milk after being fed. There were no other complaints.

Examination revealed an underdeveloped and nourished six months old female, not acutely ill. The only positive finding was the presence of a raised, bluish, exoriated mass about 3 cm. in diameter in the left upper quadrant of the abdomen, the center of which for an area about the size of a dime, was ulcerated and from the base of which came a clear, odorless, colorless, watery fluid that gave no reaction with either acid or alkaline litmus paper. This mass was firmly attached to and felt as though it were a part of the abdominal wall.

Laboratory findings on admission were: Blood: hemoglobin 68 per cent; leukocyte count—18,200 with 23.5 per cent polymorphonuclears, 73 per cent small lymphocytes 2.5 per cent large monocytes and .5 per cent

\* Ryder Memorial Hospital, Humacao, P. R.

eosinophiles. Examination of the smear also revealed the presence of the gametocytes of falciparum malaria and her stool was positive for necator americanus, trichuris and Endameba coli.

Immediately following admission the patient was placed on atabrine therapy for her malaria, and an attempt was made to determine the presence or absence of a fistulous tract from the stomach to the base of the ulcerated area. Methylene blue was twice placed in the infant's formula and the dressing was carefully watched for blue stains. None were ever seen although blue stains were found on her diapers. Several days after admission the mass began to bleed slightly so that for the next week the escaping fluid was of a serosanguineous character. In addition to this the ulcerated area became infected, began to increase in size and the patient became jaundiced as a reaction to the atabrine. She continued vomiting two or three times and having six to eight watery, foul-smelling stools daily, so that by March 22, 1941, in spite of all therapy, the infant was markedly dehydrated and running a temperature of 104°F., she previously never having had a temperature over 100°F. A transfusion of citrated blood and some intravenous saline was given and the patient's temperature returned to 100°F. by the next day. However, the vomiting and diarrhea persisted and the ulcerated area increased in size and became about 4 cm. in diameter and 1.5 cm. in depth. On March 28, 1941, a biopsy was taken with two pieces of tissue being removed, one from the wall of the ulcer, the other from the very base. The specimen was sent to the pathologist\* from whom on April 16, 1941, we received the following report:

"*Gross:* There is one elliptical fragment of tissue measuring 1.3 X 0.5 cm. It presents on its external surface towards one edge slightly raised and whitish tissue. Towards the other edge there is a finely wrinkled epidermis. Transections reveal light greenish thick corium with, towards the subcutis, circumscribed more translucent gray areas. The smaller tissue fragment does not exceed 0.8 cm. in greatest diameter. It appears to be covered largely by normal appearing epidermis. The corium is thick and gray white.

"*Microscopic:* There is one section of skin which reveals towards one border an extensive

ulcer presenting but a necrotic superficial layer with polymorphonuclear infiltration. Beneath it there is rather scanty granulation tissue with scattered polymorphonuclear reaction. There is, however, deeper fibrosis which extends into and involves the subcutis. There is another tissue fragment which is covered by a gastric type of mucous membrane. It includes as well as the mucous membrane some of the submucosa.

"*Diagnosis:* Ulcer with chronic inflammation; stomach-allantoic rest?"

On the basis of the biopsy finding of stomach tissue at the base of the ulcer, and believing that we were dealing with a fistula extending into the stomach, operation was decided upon in spite of the infant's poor physical condition. (Fig. 1.) Under drop ether anesthesia, operation was performed on April 18, 1941, at which time the abdomen was opened through a high, right rectus muscle splitting incision. On palpating the upper abdominal cavity a rounded mass about the size of a golf ball was felt attached to the anterior abdominal wall at the site of the ulceration. This was freed by blunt finger dissection and on delivery through the wound was found to have a small, nipple like opening which was the site of attachment to the base of the ulcerated area and from which the clear watery fluid was escaping. The mass itself was cystic and was continuous with the stomach wall being attached to it along the greater curvature about 3 cm. from the pylorus. This was resected from the stomach, a portion of whose wall was removed along with the cystic mass. The opening in the stomach was closed with two rows of continuous No. 0 plain catgut and one row of black silk inverting sutures, following which, the abdomen was closed without drainage. The ulcerated area, the base of which was peritoneum with a small opening, was then packed with iodoform gauze and a dry dressing was applied.

Dr. Krakower's report on the specimen was as follows:

"*Gross:* The specimen is characterized by a more or less tower-shaped cystic portion of tissue, the base of the tower being represented by a flap of gastric mucous membrane. This flap of tissue measures 3 X 2 cm. and presents several fairly thick rugae but otherwise pale intact mucous membrane. The cyst itself measures 2.5 X 2.5 X 2 cm. It is covered by serosa which is fairly smooth except for adhe-

\* Dr. Cecil Krakower, School of Tropical Medicine, San Juan, P. R.

sions about one edge of the fundus of the cyst. This edge contains a small outpouching granular portion of tissue with an orifice which

opposes the stomach proper there is a common external musculature. The mucous membrane of the stomach proper is essentially of fundal



FIG. 1. Photograph taken in the operating room immediately before operation; weight nine pounds two ounces; age seven months. Note size and depth of the mass with the ulcerated center in the left upper quadrant of the abdomen and the poor general physical condition of the baby.

leads into the tower-shaped cyst itself. Sagittal section through the specimen reveals a thick rugose mucous membrane lining the cyst, a well defined submucosa and a muscular coat clearly outlined and which serves as common musculature for the fragment of stomach as well as of the cyst where these two are opposed. There is no communication between the cyst and the stomach proper.

**"Microscopic:** The cyst is essentially a stomach in miniature. The mucous membrane is fairly thick. The glands reveal a long luminal portion made up of clear mucous cells. The shorter basal portions of the glands are made up of both peptic and oxytic cells. There are a muscularis mucosa and outer muscular coat. The latter is thick. There is some fibrosis of the adventitial tissues. In the region where the cyst

FIG. 2. Photograph taken ten minutes after baby succumbed. Weight seven pounds eight ounces; age eight months. Note the extreme emaciation and the nicely and almost completely healed and epithelialized abdominal lesion. Operative scar is barely visible just to right of the scar edge in the right upper quadrant.

character with abundant oxytic cells. There are also portions of the mucosa that are heavily infiltrated by round cells.

#### "Diagnosis: Enterocystoma."

Postoperatively, the patient took water and small quantities of diluted milk well and without diarrhea for about five days but, as soon as the milk in the formula was increased, her diarrhea reappeared. Cow's milk was then replaced by a protein S. M. A. formula which the infant took and tolerated well for about ten days following which time she again developed a diarrhea which no medication could control and which at times consisted of ten copious, watery, foul smelling stools in twenty-four hours. Meanwhile, she was steadily losing weight so that by May 1, 1941, she weighed but 7 pounds 15 ounces. The wound itself had healed nicely and the ulcerated area had granulated in so rapidly that it was now only the size of a twenty-five cent piece. The formula

was varied in strength several times with no beneficial effect on the diarrhea and on May 20th, an evaporated milk formula was pre-

narrowing this portion of stomach which is situated approximately 2.5 cm. from the pyloric end. The adhesions described above are



FIG. 3. Low power photomicrograph of biopsy specimen removed from base of ulcer showing the gastric type of mucosa and submucosa.

scribed. At this time the child was markedly emaciated and weighed but 7 pounds 8 ounces, but the abdomen was almost completely healed, there remaining nonepithelialized only a small area, about the size of a pencil lead near the center of the formerly ulcerated area. (Fig. 2.) The following morning she suddenly became worse, her pulse became weak and thready, her respirations jerky and rapid, her skin cold and clammy and at 11:45 A.M. succumbed.

Autopsy, performed twenty-seven hours after death,\* revealed no other congenital malformations, showed the resected area of the stomach to be well healed and, outside of the marked emaciation and inanition, no gross pathological condition. The abdominal viscera were removed *in toto* and sent to the pathologist whose report follows:

*Gross:* Liver, spleen and gastro-intestinal tract are received en masse. The stomach has been opened prior to submission. It reveals a fairly smooth serosal surface except for some adhesions on the anterior surface close to the greater curvature at the pyloric end. The operative area is not clearly identified. On the inner aspect the mucous membrane is granular except near the pylorus where there is an elevated area made up of closely placed small rugae. This area measures approximately 2.5 X 1 cm. It projects into the lumen greatly



FIG. 4. Low power photomicrograph showing the common muscular wall above which is the gastric type of mucosa which lined the enterocystoma and below which is the mucosa of the stomach proper.

in relation to this area. In addition there is a thick band of adhesions running between the cystic end of the gall bladder and the transverse colon. Transections through the thick polypoid area reveals it to be the probable operative site with apparently two folds of the stomach brought together and inverted. The pancreas is poorly preserved and reveals some peri-pancreatic thickening. At the head of the pancreas there is a large apparently thrombosed blood vessel. The duodenum is poorly preserved and partly wrapped by the pancreas. The small intestine and colon are not very remarkable. They contain a small amount of soft light yellowish or greenish flocculent contents. The spleen measures 4 X 2.5 cm. and weighs 10 Gm. The capsule is smooth. The pulp is light brown and the follicles are fairly prominent. The liver measures 13 X 7 X 2 cm. and weighs 130 Gm. The capsule is fairly smooth. Transections reveal poor preservation. The markings are more or less obscured. The surfaces are light brown.

*Microscopic:* All the sections reveal advanced postmortem autolysis. *Spleen:* The follicles are rather small and inactive. The pulp is cellular. There is considerable hemosiderin. *Pancreas:* There is advanced autolysis. The same applied to the adherent portions of *duodenum*. *Liver:* Is atrophied. *Stomach:* In the region of operative area there is irregular

\* Family did not come to claim body until the day following death.

adventitial fibrosis associated with areas of granulation tissue heavily infiltrated by round cells and associated with foreign body reaction. In these regions of stomach there are some mucosal glandular cysts. In some places there is also evidence of a stitch abscess in the adventitial tissues of the operative area. Elsewhere the sections of stomach are not very remarkable. *Small intestine:* Is not very remarkable. *Large intestine:* Is not very remarkable as far as one can tell. There is apparently some lymphoid hyperplasia of some of the abdominal lymph nodes.

"*Diagnosis:* Localized abscess; surgical wound of stomach."

#### COMMENT

This case presents several interesting features and complications foremost among which is the ulcerated lesion on the abdominal wall. This ulcerated area kept progressing in size despite all efforts on our part until the source of the irritating fluid was eliminated, and as soon as the enterocystoma was removed all the irritation and infection cleared up, the ulcer began granulating in freely and in thirty-three days was almost completely epithelialized. In addition, this ulcer, which would not have been present had not the originally noted abdominal mass been promiscuously incised, was the means of our deciding to operate. Without the finding of stomach mucosa and submucosa at its base laparotomy would not have been performed as we could not establish any definite connection between the stomach and the abdominal wall; and, even though the fluid resembled gastric juice to the naked eye, the baby's condition was such that we would not for diagnostic purposes alone have risked an exploratory operation. The question may arise as to whether or not we waited too long in taking a biopsy; but in the presence of the serosanguineous and later purulent discharge and our not having definitely excluded the possibility of the mass being a malignancy of the muscles of the abdominal wall, we considered it wiser to attempt clearing up the infection somewhat prior to taking tissue sections.

This delay, we believe, paid dividends as the red, nipple-like bit of tissue which we removed from the base of the ulcer and which microscopically was stomach mucosa did not appear until three days before the biopsy was performed; and we are sure that had this procedure been carried out earlier, the pathological diagnosis would have been "ulcer with chronic inflammation" and the baby would have never been operated upon and the diagnosis would not have been made prior to autopsy.

The second, a less interesting but more complicating feature and the cause of our grief and the patient's death, was the persistent diarrhea which nothing could control. For this diarrhea, whose etiology is unknown, we tried everything and every régime recommended but nothing seemed to help. It was just a losing battle from the beginning with the infant getting well surgically but continually losing ground and eventually dying of inanition. This type of diarrhea, which is common in the tropics, is a leading cause of infant death in Porto Rico where it takes a toll of 250 to 350 infants under two years of age monthly.\* This was an unwelcome complication and we are certain that without this diarrhea we would now be reporting a living and not a dead case.

The third complicating feature was the finding of the gametocytes of falciparum malaria during the routine blood smear examination. Even though the malaria had no marked ill effects on the infant, it was an extra malady for the baby to combat and was another condition for us to treat before attempting to do too much about the abdominal lesion itself.

Lastly, the routine first and then a check stool specimen showed the presence of necator ova. Although not too rare an occurrence, it is unusual to find hookworm in a six-months old baby especially in one who has not yet crawled. We are quite certain this infant never crawled as she was too small and weak even to attempt

\* Figures from the monthly reports published in the Puerto Rico Health Bulletin.

crawling. The source of the infestation was possibly some soiled toy or contaminated water as the baby was receiving nothing else by mouth except the mother's breast.

#### SUMMARY

1. A rare case of enterocystoma with duplication of the stomach is presented.

2. There was present as a complicating feature a draining ulcerated lesion on the abdominal wall which at first was the cause of much alarm and speculation but which eventually led us to the diagnosis.

3. A persistent diarrhea of unknown etiology was the most difficult therapeutic problem and eventually the cause of the patient's death.

4. This case was also complicated by the infant's having falciparum malaria on admission.

5. Also unusual was the finding of hook-worm infestation in a six-months old baby.

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# METASTASIS TO THE HUMERUS FROM CARCINOMA OF THE RECTUM\*

SYDNEY D. WESTON, M.D.

Associate Proctologist, Beth Moses Hospital

BROOKLYN, NEW YORK

WHEN this complication first presented itself, it occurred to the writer that he had never seen a metastasis to the humerus arising from a carcinoma of the rectum. The literature was scanned and 190 articles on the subject were reviewed. It was the lack of findings which caused me to report this case. Skeletal metastasis from carcinoma of the rectum is not infrequent, but metastasis to the humerus is rather uncommon. Our investigation of the literature disclosed only five reported cases of such spread. The first case of bone metastasis from rectal carcinoma was reported by Curling in 1870. This was a case of metastasis to the upper part of the radius. The first case of metastasis to the humerus was reported by Pitts in 1891, presenting itself as a spontaneous fracture of the right humerus, eighteen months after colostomy. Aufses reported a second case in 1930. In 1936, Geschickter and Copeland reported a right humerus involvement and Hayden one of the left humerus. Brown and Warren reported still another case in 1938. In Bacon's series of 318 cases with fifty-nine bone metastases, there were no cases of spread to the humerus. Skeletal metastases occur late because carcinoma of the rectum is known to spread slowly. When presenting his paper on metastasis in rectal carcinoma before the American Proctologic Society in 1940, Mechling stated that metastasis is orderly and predictable when confined to the lymphatics. It begins in the lymphatic system and goes retrograde when blockage occurs. Blood borne metastasis occurs via the thoracic duct, or by encroachment locally on the blood vessels.

Blood borne metastasis lodges in organs having a slow current (as bone) or a slow venous pulse (as liver). In discussing Bacon's paper, Mechling asserted that bizarre spread is due to the blood stream: (1) by direct invasion, (2) secondary embolization (e.g., lodging in the lung with secondary growth and spread from there), (3) passage of a single cancer cell through the lung capillaries and into the general circulation. Brown and Warren state that the metastasis via the blood stream is proportionate to the stage of differentiation. Sections of the cancer should be scrutinized carefully for evidence of intravascular tumor invasion. Presence of the latter denotes the probability of visceral spread. Absence rules it out. Yeomans in his volume on Proctology reports 320 cases with metastasis present in seventy-four, but none to the humerus.

## CASE REPORT

B. M., a white female, age sixty, first consulted us on March 13, 1940, complaining of rectal bleeding, tenesmus and loss of weight. Her personal history was essentially negative. She was married for twenty-five years. She was never pregnant. Her menstruation started at the age of thirteen, came regularly every twenty-eight days and lasted from three to four days. She had her menopause ten years ago. Her family history was essentially negative. Her past history was negative both surgically and medically.

A review of her systems revealed the following: No hemoptysis, chest complaints, dyspnea, nor precordial pain. Her appetite was good. There was no nausea nor vomiting and no constipation before her present illness. There was no frequency and no pain or burning in urina-

\* Read before the New York Proctologic Society, November 28, 1941.

tion. Her neuromuscular system was normal and venereal disease was denied.

The patient complained of bleeding per rectum since the preceding July. This bleeding would take place with defecation. She received x-ray treatments from September 6 to November 1. She complained of a "pulling down" sensation and constant pain, associated with a feeling of always wanting to move her bowels. She lost eleven pounds in weight.

Physical examination revealed no abnormalities except for a discoloration of both legs and feet. Varicosities were present. There was a cauliflower mass involving the entire circumference of the rectum just below the rectosigmoid junction which bled freely. The lumen was markedly narrowed. A biopsy was taken.

The pathological report stated that the gross specimen consisted of two hemorrhagic masses of tissue received in formalin. The microscopic report stated that the masses consisted of rectal mucosa and granulation tissue. The latter was infiltrated by atypical glands showing a moderate degree of atypism with many mitotic figures. Diagnosis: Adenocarcinoma of the rectum.

Radical surgery was advised which was promptly and definitely refused. She had been told about "electricity," and that was what she wanted. Accordingly, she was hospitalized on March 14, 1940, and the mass was electro-dessicated. After a week's stay in the hospital, she returned to her home. At intervals, she would visit us at the office at which times further superficial electrodesiccation would be instituted. The patient gained weight, and despite the marked narrowing of the lumen, apparently had little difficulty with bowel action.

During the summer of 1941, the patient began complaining of pain and some swelling of her left elbow. Believing it to be an attack of arthritis, she was referred to a medical man who treated her with no relief whatsoever. The diagnosis was finally made when x-rays were taken. These examinations revealed a metastatic deposit in the lower end of the left humerus. Radiographic examinations of the chest, skull, abdomen, right elbow, humerus and pelvis were negative. She received deep ray therapy daily, apparently without any relief, and started to go down hill rapidly. She expired on October 19, 1941.

## CONCLUSIONS

1. Metastasis to the humerus from carcinoma of the rectum is rare.
2. The prognosis is extremely grave.

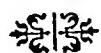
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# DOUBLE SEPTICEMIA FOLLOWING PROSTATECTOMY TREATED BY THE KNOTT TECHNIC OF ULTRAVIOLET BLOOD IRRADIATION

## CASE REPORT

E. W. REBECK, M.D.

General Surgeon, Shadyside Hospital

AND

R. A. WALTHER, M.D.

Urologist, Shadyside Hospital

PITTSBURGH, PENNSYLVANIA

THE use of the Knott technic of ultraviolet blood irradiation in acute infections has been reported by Hancock and Knott,<sup>1</sup> Barrett,<sup>2,3</sup> Miley<sup>4,5</sup> and Rebbeck.<sup>6,7</sup> The publications of these writers give the rationale and technic of this form of therapy as well as the authors' experiences with it in various pathological conditions of an infectious nature.

The literature on the subject does not disclose that a case of double septicemia involving *Escherichia coli* bacillus and hemolytic streptococcus had ever been treated with this therapy.

A case of this nature occurred in the writers' practice which was treated with ultraviolet blood irradiation and which had a satisfactory conclusion. The various factors, including the patient's age, that influenced the course of the infection and the apparent results following treatment make it of sufficient interest generally to merit reporting.

## CASE REPORT

Mr. B., No. 83857, age seventy-six, was admitted to the Shadyside Hospital on March 25, 1940, for the service of Dr. R. A. Walther. The patient gave a history of increasingly difficult passage of urine over the past year with frequency and nocturia. An admission diagnosis of prostatic hypertrophy was made. Admission blood count showed: 3,870,000 red cells, 14.4 Gm. hemoglobin, 19,750 leukocytes 54 per cent filamented, 25 per cent non-filamented. Blood urea was 26 mg., and blood sugar 108 mg. Urine showed acid reaction, 1.010 specific gravity, much albumin, very many red blood cells and a moderate number of

white blood cells. The admission temperature was 98.4°F., pulse 74, respirations 20. His general nutrition was good for a man of his age.

*Cystoscopic examination* was performed on March 26, at which time examination revealed a bladder holding 24 ounces of thick, bloody urine; the fundus of the bladder was negative except as a part of the general trabeculation; no stones or growths were noted. Openings of the ureters were not seen because of a very large ball-valve prostatic enlargement. A Foley catheter was placed in the bladder for continuous drainage. By March 29, the urine had cleared; the blood urea had come down to 15 mg. per 100 cc. His general condition seemed satisfactory for operation.

A suprapubic cystostomy was performed on this date; drainage was secured through the bladder wound with a No. 24 mushroom catheter; the Foley catheter had been removed. His progress was uneventful from this operation. Blood urea on April 1, was 10.7 mg., toxemia mild, fluid balance good; and on April 5, a second-stage prostatectomy was performed through the suprapubic wound. Two lateral and two median lobes considerably enlarged were removed. Tissue examination showed these to be benign hypertrophy with chronic prostatitis. His progress was not abnormal from this point until the morning of April 8, at which time he had a severe chill with temperature rising to 105.6°F., pulse 120. His temperature receded fairly promptly to 100 within five hours through profuse diaphoresis, but another chill occurred soon, and his temperature rose again to 105.8°F. with pulse 120, respirations 28. He became quite toxic, pale, mildly cyanotic with a uriniferous odor to the perspiration. A culture taken the morning of April 8 plus a culture taken immediately before

blood irradiation that same afternoon showed *Escherichia coli* and *Streptococcus hemolyticus*. When subcultured the *Escherichia coli* showed

12, and blood transfusions of 250 cc. each on April 13, April 15 and April 17. Blood cultures were taken as mentioned on April 8, showing

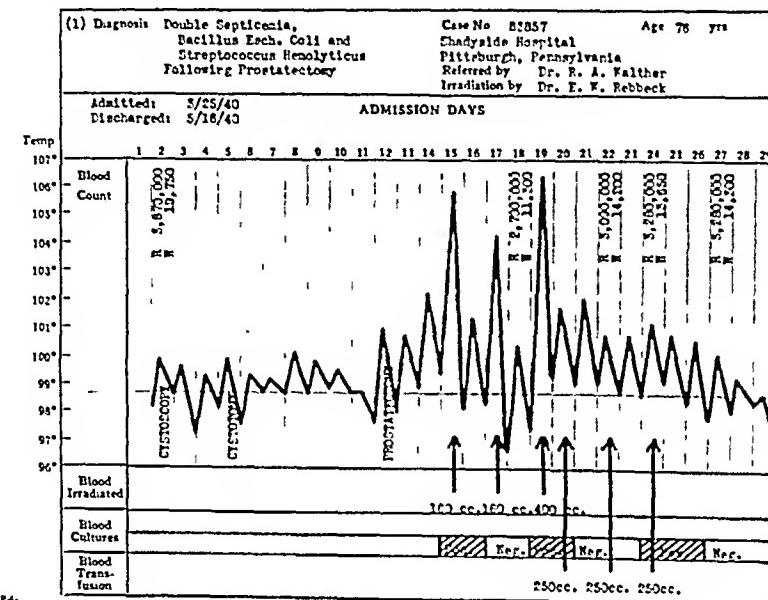


FIG. 1. Case No. 83857. Temperature graph.

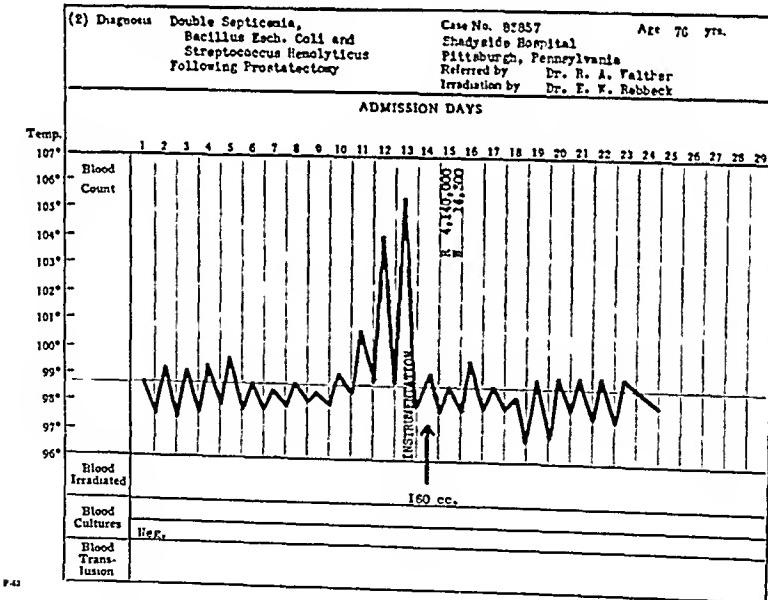


FIG. 2. Case No. 83857. Temperature graph.

profuse growth with very few of the streptococci found.

positive growths for both organisms. Blood cultures taken April 10 and 11 were negative. Blood culture taken April 12, after another severe chill showed profuse growth of *Escherichia coli* but no hemolytic streptococcus. Blood cultures taken April 14 and April 15 were negative. Blood culture taken April 17, again showed *Escherichia coli*. Blood cultures taken April 20, and May 5, were negative.

The patient made a rather uneventful recovery after April 13, until the Foley catheter was removed and replaced on May 5. This was

followed by a transient rise in temperature to 105.2°F. but promptly receded. On May 6, another blood irradiation treatment was given as a precautionary measure. The patient from this point made an uneventful recovery and was discharged from the hospital in good condition on May 16. He was last heard from by Dr. Walther in May, 1942, at which time he had apparently made a complete recovery from his operation and was in good health considering his age.

#### CONCLUSION

This case is interesting because of the fact that a double septicemia was proved by cultures, and recovery apparently ensued with no other therapy than the irradiation of autotransfused blood. No drainage of an infected focus was performed. (We have seen septicemia recovery following incision and drainage of an abscess, for example.) We do not believe that the three blood transfusions could be considered responsible for recovery from septicemia. No other specific therapy was used, with the exception of the 30 gr. of neoprontosil used just before irradiations

were started. In view of our experience with other serious infections, including septicemias, we believe the ultraviolet irradiation of autotransfused blood merits attention as a valuable adjunct in the practice of medicine and surgery.

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# CHRONIC PANCREATIC ABSCESS WITH UNUSUAL COMPLICATIONS\*

ABRAHAM J. BELLER, M.D.

AND

Attending Surgeon, Hospital for Joint Diseases

ROBERT L. NACH, M.D.

Adjunct Surgeon, Hospital for Joint Diseases

NEW YORK, NEW YORK

**S**UBACUTE or chronic pancreatic suppuration, though described in the literature, is not commonly encountered. The case reported here is of interest because of its infrequency, its preoperative duration, the misleading clinical and roentgenologic picture, the moderately severe persistent postsurgical diabetes hitherto not manifest and the terminal hepatic cirrhosis.

Steinrohn<sup>1</sup> reported a case of silent abscess of the head of the pancreas causing compression of the common duct with icterus. Bevan<sup>2</sup> and Batchelor<sup>3</sup> each have described a case of pancreatic abscess associated with cholelithiasis. Ochsner<sup>4</sup> reported an instance of an abscess in the tail of the pancreas secondary to a perforated gastric malignancy. Davis<sup>5</sup> described a case of abscess of the pancreas surgically drained in which the etiology could not be determined, the gallbladder, bile passages, stomach and duodenum being normal at the time of operation.

## CASE REPORT

J. L., a single white male, aged forty-three, a short story writer, was admitted on March 4, 1937, with a three months' history of increasing epigastric discomfort described as "gas pains," which did not radiate, which occurred frequently and irregularly at any hour, and which were not aggravated but seemingly relieved by the intake of food. For two months preceding admission, anorexia, nausea and vomiting were experienced. The vomitus contained no free blood or coffee-ground material. The stools had been allegedly tarry at times, but there was no constipation or diarrhea. There had been increasing weakness and a loss of twenty pounds in weight.

For the past ten years he had been in the daily habit of consuming excessive amounts of alcoholic beverages. At irregular intervals he would complain of epigastric distress and indigestion which were successfully relieved by simple measures. Routine urinalyses at no time had revealed the presence of any glycosuria.

Physical examination disclosed an emaciated, cachectic-looking patient who appeared ten years older than his age, and who gave the impression of suffering from a malignant disease. Temperature was 99.8°F., pulse 80, respiration 20. Physical findings were essentially negative except for a nontender, enlarged liver which extended three fingers' breadth below the costal margin, its edge being smooth and rounded. There was no palpable epigastric mass or tenderness. The sclerae were not jaundiced. The urine contained 0.3 per cent sugar. A complete blood count examination showed 4,800,000 red blood cells, 13,100 white blood cells, 79 per cent segmented neutrophiles and 16 per cent lymphocytes.

A gastrointestinal series taken shortly before admission was reported as follows: "A large filling defect was noted in the pars media with narrow canalization. Another defect in filling was noted in the pars pylorica. (Fig. 1.) No peristaltic activity was visualized over the involved area. A localized tender point was found over the sites of the filling defects. Mobility of the stomach was limited. At six hours, the stomach was completely emptied and the head of the meal was in the splenic flexure. The Ewald test meal, removed one hour after administration, furnished a clear fluid secretion which was definitely hyperacid. The findings are those of a filling defect in the pars media and the pars pylorica. The rapid evaeuation through a gaping pylorus indicates the probability of a seirrrous carcinoma. The hyper-acidity found in the gastric secretion is of questionable significance as the patient ad-

\* From the Surgical Service of the Hospital for Joint Diseases, New York, New York.

mitted to having taken some wine just prior to administration of the Ewald test meal."

Abdominal exploration performed on March

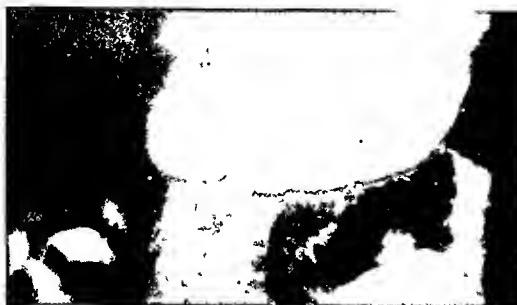


FIG. 1. Filling defect of the stomach involving the pars pylorica and pars media.

6, 1937, under gas-oxygen-ether anesthesia showed the stomach to be normal in size and shape and to be free of any mass or defect as preoperatively diagnosed. There were no perigastric or cholecystic adhesions. The gallbladder, slightly enlarged but normal in appearance, contained a number of small calculi. The common duct was not dilated and did not appear to contain any calculi. The liver which was yellow-brown in color was enlarged to about one and one-half times the normal size. The lymph glands along the lesser curvature of the stomach were enlarged and the tissues of the gastrohepatic omentum were swollen and edematous. A large, fixed, firm mass was felt posterior to the stomach. The lesser peritoneal cavity was entered into by incising the gastrocolic ligament. It was difficult to determine whether the lesion was in the pancreas or retroperitoneal tissues, or whether it was inflammatory or neoplastic in character. An incision made directly over the center of the mass released a small amount of yellowish-white fluid resembling pus. An operative diagnosis of pancreatic suppuration was made. Cigarette drains were inserted down to the pancreatic area through the previously made opening in the gastrocolic ligament. The gallbladder was opened and the calculi were removed. Because of the nature of the pathological condition, it was deemed advisable to establish temporary drainage of the biliary system by means of a cholecystostomy.

The immediate postoperative reaction was good. On March 11th, the urine was found to contain 4 per cent sugar and 2 plus acetone; the blood contained 255 mg. of sugar per 100 cc. He was placed on a diabetic regimen of carbo-

hydrates 120, proteins 70, fat 60, and two daily 15 unit doses of insulin. On March 13th, a moderate purulent discharge appeared along the abdominal drains. At the same time urinary retention occurred, making it necessary to insert an indwelling catheter into the bladder. Daily maintenance doses of whiskey were given to avoid an alcoholic psychosis. On March 17th, a severe sloughing fascial infection with disruption of the abdominal wound was noted. The abdominal viscera presented, but they were firmly adherent to the peritoneal edges and no evisceration occurred. The patient's general condition remained good and the diabetes was readily controlled. The cholecystostomy tube and indwelling catheter were removed on March 19th. He was discharged from the hospital on April 16th with the wound healed, but with some persistent biliary drainage which ceased after two weeks.

Culture of the pus from the pancreas was positive for *Staphylococcus aureus*. The pathological specimen consisted of numerous small gallstones about 0.5 cm. in diameter which were soft and consisted principally of bile pigment. A fragment of tissue from the gastrohepatic omentum consisted of inflamed fat and omentum with no evidence of malignancy.

The patient maintained fairly good health with the aid of a diabetic diet and 30 units of insulin daily. He developed a large incisional hernia, approximately 8 by 10 inches in size. Because of anticipated technical difficulties that would attend the repair of such a defect in a poor operative risk, operation was permanently deferred and relief was afforded by means of an abdominal support.

In June, 1940, there was a complaint of weakness and dyspnea on exertion. Weekly consumption of 2 gallons of alcohol had persisted up to date. The sclera and skin were decidedly icteric. There was a moderate ascites, and the liver which had been definitely enlarged at the time of operation could not be palpated at this time. Ankle edema to a mild degree was present. With a daily dosage of 25 units of insulin and with a diminished food intake due to the amount of alcohol consumed there was no glycosuria. The jaundice, anorexia, ascites and ankle edema became more pronounced and on August 2nd he lapsed into a coma and died two days later. No operative procedure had been considered since the clinical condition was believed to be that of an

alcoholic atrophic cirrhosis rather than an obstruction of the extrahepatic bile ducts.

At autopsy the abdomen contained approximately 1 gallon of clear amber-colored fluid.

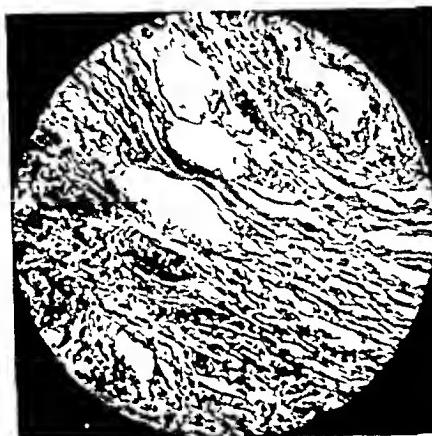


FIG. 2. Fibrosis of pancreas with pronounced replacement of the parenchyma by fibrous tissue, and almost complete absence of isles of Langerhans.

Firm adhesions held the stomach to the under-surface of the liver. Esophageal varices were present and apparently were the source of the tarry stools originally described. The liver (2,400 Gm.) appeared definitely smaller than at the time of operation three years before. It was yellowish-gray in color, had a smooth surface, and on section cut with a firm gritty feel. The gallbladder did not contain any more calculi and the extrahepatic biliary ducts were patent and apparently normal. The spleen was hyperemic, about normal size (180 Gm.), and presented no gross pathological abnormality. The pancreas was somewhat larger than normal (200 Gm.) and appeared to have undergone an almost complete replacement fibrosis. In its tail there was a residual, necrotic, thick-walled abscess cavity 1 by  $\frac{3}{4}$  inches in size. (Fig. 2.) The kidneys exhibited cortical scars of a benign nephrosclerosis. The lungs were the seat of a pulmonary edema with scattered patches of lobular pneumonia. Consent for examination of the brain was not obtained.

Microscopically, the lungs revealed evidence of pulmonary edema and bronchopneumonia. The heart presented nothing of note except for some fragmentation of the myocardial fibers. In the kidneys the glomeruli revealed occasional hyalinization scattered irregularly through the cortex. The intima and media of the smaller arteries were thickened. The tubules showed evidence of cloudy swelling

and contained some débris in their lumina. There was a moderate increase in the interstitial fibrous tissue with some focal collections of round cells.

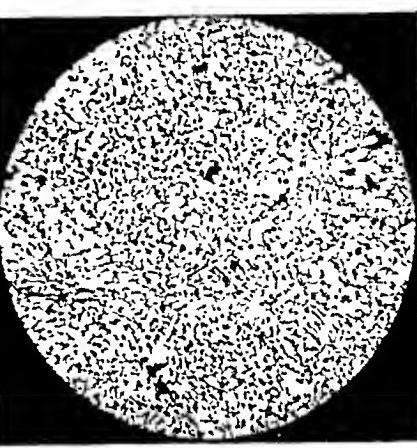


FIG. 3. Cirrhosis of liver with distortion of the architecture and pronounced fatty degeneration.

In the spleen the capsule, trabeculae and the media of the central arterioles were thickened throughout. The sinusoids were markedly congested with red cells. There was a marked increase in pigment in the reticulo-endothelial cells and an increased number of polymorphonuclear cells in the splenic parenchyma.

The liver was the seat of extensive fatty degeneration. There was a marked distortion of the parenchymal architecture with dissociation of the liver cords. An irregular increase in fibrous tissue was noted about the portal canals. The connective tissue extended irregularly throughout the substance of the liver so as to distort its structure. The hepatic ducts were increased in number and there was a moderate round cell infiltration about the portal canals. The vessels were essentially normal. The Kupffer cells were filled with bile pigment which was also present in the hepatic cells. The hepatic cells were globular, cloudy and swollen and had undergone severe fatty degeneration. In several lobules there was an attempt at regeneration of the hepatic cells. (Fig. 3.)

Marked connective tissue replacement had occurred in the pancreas throughout the glandular substance. The fibrous tissue had pinched off the few remaining groups of glands, completely isolating the glandular elements. Scattered throughout the connective tissue were focal collections and diffuse infiltrations of round cells. The residual glands appeared as cloudy areas of hyalinized acini in the sub-

stance of the fibrous tissue. The ducts were dilated and contained some amorphous material. Small areas of necrosis were irregularly

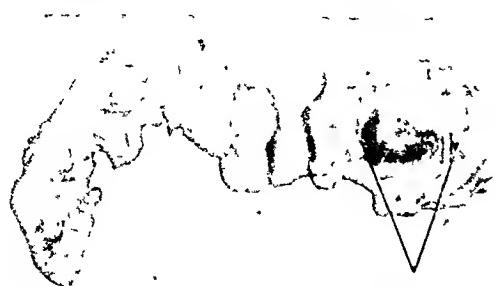


FIG. 4. Marked fibrosis of the pancreas with a residual abscess cavity in the tail.

scattered throughout. A marked diminution in the isles of Langerhans existed, the striking point being an almost complete absence of islets from the sections. The arteries and smaller vessels were essentially normal.

#### COMMENT

Most instances of pancreatic suppuration are the result of bacterial invasion secondary to acute hemorrhagic necrosis. Much less frequent are those cases of primary bacterial invasion arising either by (1) extension from an adjacent organ by contiguity or through the lymphatics, (2) via the blood stream, or (3) by way of the biliary or pancreatic ducts. Metastatic abscesses to the pancreas are rarely seen. Although there were no recognized antecedent episodes of biliary colic or gallbladder inflammation, it is strongly suggestive that in this instance, because of the co-existing cholelithiasis, the pathogenesis may have been that of an ascending infection via the biliary and pancreatic ducts. On this presumption drainage of the potentially infected ducts was attempted by means of a cholecystostomy.

The stomach outline with its very apparent filling defect, the history of indigestion, the repeated vomiting, and the marked weight loss favored the diagnosis of a gastric neoplasm. From the degree of pancreatic enlargement found at operation and the pronounced roentgen distortion of the stomach outline it was surprising that the mass could not be

palpated preoperatively. There was no fever or chills prior to operation that might have led one to suspect a suppurative process. The moderate leukocytosis might have been considered as suspicious of an infection. The hyperchlorhydria was not in keeping with the diagnosis of a gastric malignancy, but one would not dare rule out the latter lesion because of this discrepancy, especially in the presence of the pertinent signs and symptoms described above.

The development of a postoperative persistent diabetes clinically indicated that the suppuration must have involved a major portion of the gland, and that the amount of active parenchyma destroyed by such inflammation was considerable. Allen,<sup>6</sup> offering experimental data, has shown that a definite relation exists between the amount of pancreatic tissue allowed to remain in the body and the degree of glycosuria. Where one-fourth or more of the pancreas is left, no glycosuria will follow. A residue of one-sixth of the gland will result in a mild transient diabetes. When one-eighth of the gland is allowed to remain, temporary severe or mild permanent diabetes is the usual result. Hence, it was believed that at least seven-eighths of the pancreatic islets had been destroyed or had undergone a degenerative change as a result of the suppuration in this case. The subsequent pathological examination substantiated this impression, as evidenced by the diffuse fibrosis, the residual abscess cavity, and the almost complete absence of the islets of Langerhans. From the location of the residual abscess cavity, it appears that the original suppurative lesion involved the body and tail of the pancreas. Opie<sup>7</sup> showed that the pancreatic islets were more abundant in the head of the pancreas.

Experimentally, the pancreas has been shown to possess a specific fat metabolizing hormone, the absence of which is productive of severe fatty degeneration and infiltration in the liver. It has been noted by Alan et al.,<sup>8</sup> and by Dragstedt et al.<sup>9</sup> that

completely depancreatized dogs, though adequately treated with insulin, would usually die within two or three months and that the outstanding findings were the fatty infiltration and degeneration of the liver. Such changes could be prevented or retarded by the addition of fresh raw pancreas to the diet. The pancreatic hormone having the power to prevent these degenerative liver changes and permit the survival of the depancreatized animals is soluble in alcohol, 5 per cent sodium chloride and water, and is insoluble in ether or pancreatic juice. This hormone has been termed lipocaic by Dragstedt.

There is a definite correlation between the clinical course and pathological findings both in this case and in the depancreatized animals. The diffuse fibrosis in this instance might be considered to be the equivalent of a pancreatectomy. It is difficult to be certain whether the histological changes in the liver are the result of chronic alcoholism, or whether they are, in whole or in part, due to the fibrous replacement of the pancreatic parenchyma with the consequent interference with the fat metabolizing hormone lipocaic. Ordinarily, histological studies of atrophic portal cirrhosis do not reveal the fatty degenerative changes in the liver as seen both in this case and in the depancreatized animals.

#### CONCLUSIONS

It is believed that this case is worthy of note for the following reasons: (1) The

presence of a chronic pancreatic abscess, a condition seldom encountered and but scarcely described in the textbooks or current literature; (2) the mistaken clinical diagnosis due to misleading clinical signs and roentgen findings; (3) the development of diabetes mellitus, clinically indicating the destruction of at least seven-eighths of the pancreatic islets, this being substantiated by the postmortem findings; (4) the postmortem findings which disclosed extensive pancreatic fibrosis with a residual abscess cavity, and a cirrhotic liver with unusually severe fatty degeneration; and (5) the degenerative changes seen in the liver closely resemble those that occur in the depancreatized animals, and which are interpreted as being due to the absence of a specific pancreatic fat metabolizing hormone termed lipocaic.

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# ECHINOCOCCAL CYST (HYDATID) OF SPLEEN AND LIVER

## REPORT OF TWO CASES

CARL R. STEINKE, M.D.

Visiting Surgeon, City Hospital; Consulting Surgeon, Children's and St. Thomas Hospitals  
AKRON, OHIO

**E**CHINOCOCCAL (hydatid) cysts in the human being are uncommon in Canada and the United States of America, as there is an average of from 3 to 5 cases reported each year and rarely is one of these a native born American. Practically all cases are immigrants from Iceland, Germany, Russia, Greece, Great Britain or Italy. The condition is also frequent in Australia, Argentina and Uruguay.

Two cases seen within two years of each other and the only cases operated upon by the author in thirty years of practice are interesting. One occurred in the spleen with secondary cyst in the omentum, while the other was in the left lobe of the liver.

Brailsford<sup>1</sup> says "It is obvious therefore, that the faeces of an infected dog may possess an enormous number of ova. These ova, having been swallowed, are attacked by the gastric juice which dissolves the ova shells and sets free embryos having 6 spines. These embryos obtain access to radicles of the portal vein and are carried to the liver. In the liver most of the embryos settle and develop into hydatid cysts but a proportion get through into the general circulation via the inferior vena cava and the right heart from which they are carried to any tissue of the body, where they ultimately come to rest and develop into hydatid cysts."

In man, of each one hundred cases, approximately seventy appear in the liver, ten in the lungs, two and five-tenths in the kidneys, two and five-tenths in the spleen, five in other abdominal organs, five in the muscles, four in the brain and one in the bone, according to Brailsford.

Daughter cysts, it is believed, develop following trauma to the parent cyst, as

those of the bony thorax or skull are generally single.

Many cases simulate gallbladder disease, with pain and jaundice when the lesion is in the liver, making the diagnosis very difficult in this country where hydatids are not suspected.

The diagnosis may be made by the Casoni intradermal skin reaction test or the Magath scratch cutaneous test which are present even after the cyst is dead or has been removed. The complement fixation test is positive in 85 per cent when the cyst is still living but not after removal of the cyst. Calcification may wall off the parasite so it will give no further trouble. Eosinophilia is noted when the cyst has ruptured or when there is absorption from its contents.

Adequate surgery is the only treatment for cure. Some writers advise injecting 2 to 10 per cent formalin into the cyst before it is opened to kill the daughter cysts and sterilize the fluid. The sac may be removed and the cavity closed or it may be swabbed out with phenol, marsupialized or freely drained.

## CASE REPORTS

**CASE I.** J. M., born in Hungary, aged thirty-two years, as a boy had a number of dogs as pets. Sheep were raised in the country and he said many died from echinococcal disease. He was in the Hungarian Army during the first World War, serving in Albania and Turkey. However, he thought the present trouble started during 1922, while serving in the cavalry in Yugoslavia. He came to the United States in 1929.

In July, 1930, he began to notice intermittent pain in the left upper quadrant which radiated to the back, accompanied by the loss

of weight and strength. By March, 1931, the pain was continuous and he began to have nausea with vomiting.

When seen April 7, 1931, by Dr. George E. Chittenden, at the Akron Clinic, his skin was lemon yellow in color and the sclerae were rather yellow tinged. All his teeth had been removed previously. He had lost fifty-two pounds in weight, was down to 178 pounds, and was weak. His heart and lungs seemed in good condition. The pulse was 76 and the blood pressure by mercury manometer was, systolic 100 mm., diastolic 70 mm. There was a distinct, tender tumor in the left upper quadrant, rather difficult to outline, extending about 2 inches below the costal border. The right lobe of the liver was enlarged and palpable. The remainder of the examination was essentially negative.

The blood count was: red blood cells, 3,960,000, hemoglobin 78 per cent, white blood cells 17,000, with 73 per cent polymorphonuclears, 23 per cent small lymphocytes, 4 per cent large monocytes. Counts in St. Thomas Hospital on the 8th and 14th of April, were about the same with only one eosinophil being reported. The icteric index was 10. The urine was dark amber, acid, specific gravity 1020, bile positive, 4 plus albumin and no sugar. There were many granular and waxy casts with a few white blood cells. Phenosulfonephthalcin test gave 56 per cent return in one hour.

A flat roentgenogram of the abdomen showed a large mass in the left upper quadrant. X-rays of the chest, skull and femurs seemed normal, with no sign of metastatic malignancy.

Cystoscopic examination with pyelogram by Dr. Chittenden revealed an obstruction to the left ureter about 18 cm. from the bladder with the urine flow from the left kidney difficult to establish. The flow from the right kidney was normal. Pyelogram of the right revealed slight enlargement, while the left showed marked deformity of the upper and middle calices with rather typical spider-legged upper calyx. He was admitted to St. Thomas Hospital the same evening.

He was operated upon by the author on April 10, 1931, under ethylene anesthesia, through a left rectus incision. The spleen was found greatly enlarged and firmly adherent to the undersurface of the diaphragm postero-laterally. The spleen was freed gradually, the pedicle exposed, clamped, cut and tied. In the

upper posterior part of the spleen was found an echinococcal cyst about 4 inches in diameter, in which there were many daughter cysts. These cysts and the large cyst wall were removed along with the spleen. A stab wound was made to the left of the incision and 2 eigaret drains inserted. The reetus incision was closed in layers. A transfusion of 550 cc. of whole blood was given, as there was considerable bleeding and shock. The temperature rose to 38.6°c. on the second postoperative day, and returned to normal by the sixth postoperative day. The pulse and respiration did not noticeably vary. He made a good recovery and left the hospital April 26, 1931.

The pathological report confirmed the diagnosis of echinococcus (hydatid) cyst of the spleen with many hooklets.

On September 18, 1936, he was sent into the City Hospital of Akron, by Dr. Roy G. Pearce of the Akron Clinic with abdominal pain and vomiting of five days' duration. The patient had noticed a mass in the right side of the abdomen for one year. The mass had grown gradually and now was about 5 by 7 inches across, hard and only slightly movable. There had been no blood noticed in the stools, but he had been constipated. The heart and lungs revealed nothing abnormal. The temperature was 100°F. rectally, pulse 96 and respiration 20. He was pale but well nourished. The erythrocytes were 2,180,000, hemoglobin 7.5 gm. per 100 cc. of blood, leukocytes 12,600, neutrophils 52, small lymphocytes 46, eosinophils 2. The coagulation time was three minutes and thirty seconds. Urinalysis showed 3 plus albumin (4 gm. per liter), occasional leukocyte, erythrocyte, granular cast and epithelial cell. The blood pressure was 180 mm. of mercury systolic, and 90 mm. diastolic. The blood Wassermann was negative.

A gastrointestinal x-ray study was made revealing a large semi-opaque mass in the right side of the abdomen, pushing the gastrointestinal shadows to the left. Knowing the previous history, this shadow was diagnosed as echinococcal cyst, likely retroperitoneal.

A transfusion of 500 cc. whole blood was given September 23, and operation by the author performed the same day under nitrous oxide, oxygen, ether vapor anesthesia. Through a right rectus incision an echinococcal cyst of the omentum about 5 by 7 inches was removed without rupturing it. Several small cysts over

the left side of the urinary bladder were removed. There was a large multilocular cyst at the left kidney area involving the undersurface of the diaphragm. Because of the anemia and location of the cyst it was decided to close the abdomen without drainage and reoperate later by a different approach. The incision was closed in layers. The pathological diagnosis was echinococcus cyst 21 by 17 by 10 cm. On opening the cyst clear watery fluid escaped. It was filled with small translucent cysts up to 3 cm. in diameter which contained watery fluid.

On October 3, another transfusion of 750 cc. whole blood was given and operation performed through a left subcostal incision. The cyst, about 4 by 4 inches under the left lobe of the liver and diaphragm was gradually freed and removed. Two rubber tubes and one cigaret drain were inserted and the incision closed in layers. A good recovery followed, the erythrocytes increasing to 4,380,000 and the hemoglobin to 11 Gm. per 100 cc. of blood. The patient was discharged October 29, 1936.

He was readmitted to the City Hospital of Akron, March 11, 1938, complaining of pain in the upper portion of the abdomen, vomiting large amounts of blood and passing black stools. There was postprandial distress relieved somewhat by soda bicarbonate. The week before he began feeling very weak and collapsed once at work. He was pale and weak but otherwise seemed in good condition. The erythrocytes were 1,180,000, hemoglobin less than 25 per cent, leukocytes 9,600, with neutrophils 67, small lymphocytes 32 and transitionals 1. He was given two transfusions of 500 cc. whole blood which brought his erythrocytes to 4,210,000 and the hemoglobin to 9.5 Gm. The x-ray studies of the gastrointestinal tract were reported negative by Dr. F. T. Moore. He was discharged March 24, with a diagnosis of esophageal varices and secondary anemia.

He was readmitted December 25, 1938, stating he had been fine until the day before when he had vomited a large quantity of fresh blood, and became weak and dizzy. He was given 550 cc. of blood by transfusion and discharged January 3, 1939.

On March 14, 1939, he returned to the hospital because of weakness and vomiting of blood. X-ray studies at this time by Dr. F. T. Moore revealed a lesion suggestive of an ulcer crater in the second portion of the duodenum,

The patient refused operation. He was given another transfusion of 500 cc. of whole blood which brought the erythrocytes up to 3,740,000 and hemoglobin to 10 gm. per 100 cc. of blood. Gastric analysis was positive for occult blood, free hydrochloric acid was 25, total acid 57, and laetic acid none.

In January, 1941, he was feeling fine, eating well and gained weight up to 168 pounds. His color was good and he had been working as an orderly at the Children's Hospital of Akron.

On November 13, 1941, he was seen in the office stating he had vomited a small amount of red blood and noticed some soreness in the epigastrium and the left subcostal region. His bowel movements had been regular and normal. His color was good and the general examination revealed nothing unusual.

CASE II. H. B., a male, Italian grocer, thirty-six years of age, was admitted to St. Thomas Hospital, October 20, 1929. His parents and five sisters were living and well in Italy. He gave the history of having had trouble for about ten years with belching of gas, pain in the left subcostal region radiating to the back, with nausea and loss of fifteen pounds in weight. The attacks would come about twice a year and he would become very yellow at the time. When the pain was severe he would not be able to straighten up. The stools would be light colored following the spells of pain. He would feel hungry but was afraid to eat much because of pain about two hours after meals. The last attack occurred four days before admission. His appendix had been removed in 1917.

He had returned to Italy for examination where many x-rays had been taken and the report given him was "adhesions at the duodenum." He was getting compensation from the United States Government following his army service so had been studied at the Hines Hospital in Chicago, where a diagnosis of chronic cholecystitis with colitis was made.

On admission his temperature was 37.4°C., pulse 94 and respirations 24. He was thin but did not seem acutely ill. There was tenderness in the epigastrium and to the left with some rigidity. The abdomen was flat and no mass could be palpated. The remainder of the physical examination was negative. The urinalysis was negative. The hemoglobin was 95 per cent, leukocytes 22,400, polymorphonuclears, 91, small lymphocytes 3, large lym-

phocytes 6, and no eosinophils. The blood Wassermann was negative.

Operation was performed by the author on October 21, through a high abdominal incision. The gallbladder was greyish blue in color, distended and tense, so it was removed. The right lobe of the liver appeared about normal. The left lobe of the liver revealed a white, hard, oval-shaped area about 4 inches in diameter, extending from the upper surface through to the undersurface. Upon aspiration a clear fluid was obtained so an echinococcal cyst was suspected. The area was well packed off and the cyst opened. Literally hundreds of small daughter cysts were removed from the cyst cavity. It was lined by a wall almost cartilaginous in density, a part of which was removed. The cyst was marsupialized and left open. The abdominal incision was sutured in layers around the marsupialized area.

Pathological diagnosis was subacute cholecystitis with cholelithiasis and multiple echinococcal cysts of the liver. The cyst wall was made up of dense, loosely arranged hyaline connective tissue with a few blood vessels surrounded by calcified material.

A good recovery followed, although the wound was kept open and he left the hospital on the eighteenth postoperative day. By February 14, 1930, the wound was solidly healed.

On October 27, 1931, he was complaining of pain in the epigastrium about three hours after meals but physical examination revealed no abnormality.

He was seen again October 30, 1931, after having been studied at the Naval Hospital in Cleveland. Two different x-rays of the stomach and duodenum had been negative for ulcer. He was still having pain and distress in the epigastrium and to the left. The appetite was good and he got relief with eating or the taking of soda bicarbonate.

On February 1, 1932, he was feeling well and having very little distress. By April 1, 1939, he was having distress whether he ate or not and seemed worse about four hours after eating. He was still taking soda bicarbonate which seemed to help him.

He was seen last in the office January 2, 1942, at which time he was feeling fine, his color was good, and he had no complaints.

#### SUMMARY

1. Two cases of echinococcal cyst are reported, one originating in the left lobe of the liver and the other in the spleen with recurrence in the omentum and left sub-diaphragmatic area and upper surface of the urinary bladder.

2. One patient was a native Hungarian, while the other was born in Italy.

3. Both had symptoms greatly simulating peptic ulcer following operation but the diagnosis of ulcer could not be verified by x-ray or at operation.

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# ESOPHAGOSPASM\*

TRANSTHORACIC ESOPHAGOPLASTIC OPERATION WITH REPORT OF A CASE

HARRY E. ISAACS, M.D.

Attending Surgeon, Beth Israel Hospital

NEW YORK, NEW YORK

S PASM of the lower esophagus is probably its most common lesion excepting carcinoma. It is followed by a superimposed dilatation, depending in degree upon the extent and duration of the syndrome. The primary cause is probably an excess of stimuli through the sympathetic nerve supply, which is not counteracted by the parasympathetic and its vagal branches (Walton<sup>3</sup>). As a result of the autonomic imbalance in a reactive attempt to overcome the stenosis, the sphincter of the esophagus (Abel<sup>4</sup>) hypertrophies, as do the circular muscle fibers above the sphincter. Even though a true anatomical sphincter of the lower esophagus may not ordinarily exist, a sphincter develops in the case of prolonged spasm (Lendrum<sup>5</sup>). The outer, longitudinal muscular fibers, innervated by the vagus, which would tend to keep the esophagus open, do not hypertrophy. An important point in the surgical anatomy, is that the sphincter, primary or acquired, is at and above the hiatus in the diaphragm, below which is the short segment of the abdominal esophagus. When spasm is followed by hypertrophy of the sphincter and circular muscular fibers, the neurogenic factor is replaced by an organic change and the fusiform or pyriform dilatation progresses until the increase in length as well as width of the lower esophagus causes it to assume a sigmoid shape by rotation toward the right side where it rests on the diaphragm, the posterior portion of which is below the level of the esophageal hiatus. (Fig. 3B.) This causes a ball-valve type of block which not only adds to the original

mechanical hindrance but tends to increase (Mosher,<sup>6</sup> Mosher and McGregor<sup>7</sup>). An elongated dilated esophagus is the final stage of the lesion, with ulceration of the mucosa and atony of the muscular fibers.

Symptoms and clinical course are typically illustrated in the following case report which presents all three stages described by Plummer and Vinson:<sup>8-12</sup>

## CASE REPORT†

The patient, a thirty-five year old married woman, was first admitted to the hospital on November 27, 1935. All elements of the history were unimportant except those related to her chief complaint, which was gradual in onset. For a period of three years, eating was followed by a sense of discomfort and pressure in the substernal region which seemed to radiate upward "to the chest, the neck and to both ears." This symptom became more frequent and more severe until vomiting culminated and relieved the attack. There was no nausea.

In January, 1935, after an attack of influenza, she found it difficult to swallow cold fluids which were immediately regurgitated. Then certain solid foods were rejected, particularly the coarser vegetables and fruits. The list of foods which were not tolerated increased until in the month before admission, all food—liquid or solid—was either immediately regurgitated or was vomited within twelve hours after ingestion. Food regurgitated was unchanged in appearance and vomitus consisted of undigested food particles of one, two or three meals, mixed with a large amount of sour-smelling, frothy, whitish mucinous fluid.

Physical examination was essentially negative. The patient was an alert, intelligent,

† Presented at the Clinical Conference of The Beth Israel Hospital. Feb. 17, 1941.

\* This term is chosen since the lesion is in the esophagus and not in the stomach as the term, "cardiospasm," would imply. It does not require qualification as does the currently popular term achalasia (Hurst,<sup>1</sup> Hurst and Rake<sup>2</sup>).

woman, pale and undernourished, 5 feet 4½ inches in height, weight 98 pounds, thirty pounds below average weight before onset of

hydrogen-peroxide. Vomiting became less frequent during the eighteen-day period of Levin-tube feeding but then occurred occasionally.



FIG. 1. Roentgenogram showing characteristic appearance of lower esophagus immediately after ingestion of contrast media.



FIG. 2. Roentgenogram showing four-hour retention of contrast media.

symptoms; blood pressure 110/70; red blood cells 3,200,000, hemoglobin 50 per cent. Blood chemistry was normal. Chemical analyses of test meals showed an absence of free acid and a low total acidity. However, these examinations were of the esophageal contents since a tube was never passed into the stomach.

The roentgenogram repeatedly showed a spasm of the lower esophagus above which there was a marked dilatation with retention of contrast media. Incidentally, the duodenum showed a defect characteristic of ulcer on all examinations except in the series taken immediately before operation. At no time were there any symptoms due to this finding.

Esophagoscopy showed a narrowed distal end with marked dilatation above, containing several ounces of a stagnated, sour-smelling, frothy, milky fluid. Neither ulceration nor neoplasm was found. The lower esophagus would not permit the instrument to pass but a small-caliber, rubber-tipped bougie was pushed through the constricted portion into the stomach.

Treatment consisted of a high caloric diet through a Levin tube, daily dilatation of the lower esophagus with a Hurst mercury dilator and esophageal irrigation with a solution of

The patient was taught to irrigate and dilate the esophagus and to pass the Levin tube for feeding. Under this régime she improved, gained five pounds and was discharged six and a half weeks after admission.

From January, 1936, to March, 1939, the patient faithfully carried out the prescribed treatment. Regurgitation and vomiting occurred occasionally but there was little or no discomfort. Then swallowing became difficult, eating or drinking caused discomfort and the Levin or esophageal tube was promptly expelled. Vomiting of food and frothy mucus followed every meal. Weakness and weight loss became progressive. The patient was readmitted and after eighteen days of treatment, the symptoms abated and three of the nine pound loss in weight were regained. The patient was admitted to the hospital for the third time, for a period of five days, in June, 1939, for check-up, after which she spent three months in the country, relieved of household duties. The routine of treatment was continued with an improvement which was maintained until the summer of 1940. Then the symptoms returned: substernal pressure and pain, regurgitation and vomiting of food, weakness and emaciation. She was readmitted November 16, 1940. Physical findings were unchanged from

previous examinations except that the x-ray showed a greater degree of dilatation of the esophagus (shadow 4 cm. wide) without

sure of the dilated, thickened, redundant esophagus. The mediastinal pleura was incised and the lower end of the left side of esophagus

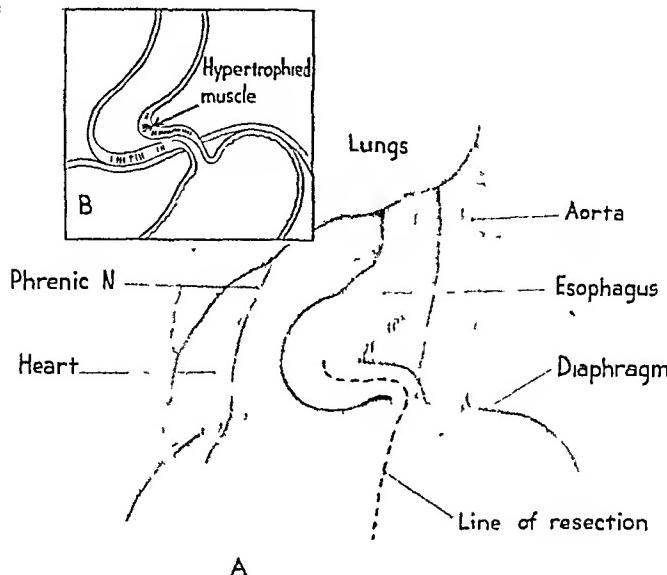


FIG. 3. A, diagrammatic relations of dilated esophagus. B, indicates site of incision through muscularis and relation of abdominal esophagus to diaphragm.

evidence of new growth or ulceration in any part of the digestive tract. (Figs. 1 and 2.)

Esophagoscopy was performed by Dr. Max L. Som on November 25th, December 23rd, December 26th, December 30th, January 2nd, January 6th and January 16th. The constricted portion of the esophagus was dilated to a diameter from 18 to 25 mm. A Tucker dilator failed to overcome the stenosis, above which there was marked distention with retention of food and mucinous secretion. The mucosa of the lower esophagus was thickened and encrusted.

Surgical consultation was held on December 17th, at which operation was advised through a transpleural incision and the probable procedure was discussed with the attending thoracic surgeon. Medical treatment was continued for another month without improvement, after which the patient was transferred to the surgical service.

Operation was performed on January 29, 1941, under spinal anesthesia. An incision was made through the tenth intercostal space from angle of rib to anterior axillary line and 1 cm. of tenth rib was resected at its angle. The pleura was opened widely through the intercostal space and an adequate field was obtained by retraction of ribs, which gave a wide expo-

sure of the dilated, thickened, redundant esophagus. The mediastinal pleura was incised and the lower end of the left side of esophagus

was mobilized to its hiatus, at which a 10 cm. incision was made through the dome of the left diaphragm, permitting delivery of the fundus of the stomach into the operative field. Beginning at the re-entrant angle indicated by arrow in Figure 3B, a 5 cm. longitudinal incision was made through the musculature, exposing the thickened mucosal layer.

The muscular layer was approximately 5 mm. thick and its appearance as well as that of the mucosa bulging through the incision was strikingly similar to the findings at operation on a hypertrophic pyloric stenosis. (Fig. 4.) The operation was considered completed at this point but an accidental tear of the mucosa occurred. The tear was repaired by a submucous suture of No. 000 plain catgut. A 5 cm. slightly curved incision, convexity upward, was made through the muscularis of the stomach at right angles to the incision in the esophagus. (Fig. 5.) The inverted T incision thus formed was closed transversely and the fundus of the stomach was brought upward and sutured over this wound. (Fig. 6.) Sulfanilamide (3 Gm.) was sprinkled over the field after which the incision in the diaphragm was sutured. The left phrenic nerve was crushed, immediately relaxing and immobilizing the diaphragm. The thoracotomy wound was sutured in layers. Air

was aspirated from the left chest until normal intrathoracic pressure was restored. The duration of operation to skin closure was fifty minutes.

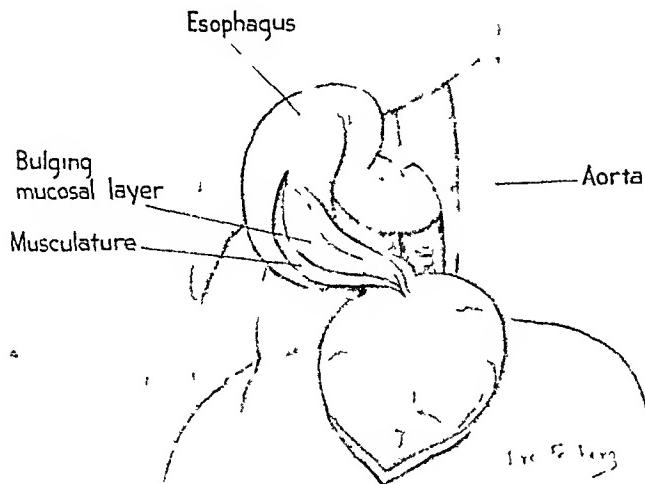


FIG. 4. Pluera over esophagus incised, fundus of stomach delivered through opening in diaphragm and incision made through hypertrophied muscle of lower esophagus

Postoperatively, a Levin tube was passed into the stomach, fluids were administered intravenously, 2,000 cc. daily for forty-eight hours, after which the patient was fed through a Levin tube in gradually increased amounts for four days. Thereafter, a fluid diet was increased to a full and unrestricted diet on the twelfth postoperative day. The temperature which never rose above 101.8°F. reached normal on the fourth day. There was no respiratory embarrassment or cough, no substernal pain or discomfort, nor any nausea or vomiting. The patient was discharged twenty-four days after operation.

At a follow-up examination April 7, 1941, the patient stated that she has had none of her previous symptoms and feels better than at any time in the past nine years. Her appetite is good; she eats everything but prefers to have vegetables pureed; her weight is 111 pounds, a gain of thirteen pounds. A roentgenogram showed a residual dilatation (1.5 cm. diameter) of the esophagus limited to the upper portion. Tone and lumen of the lower esophagus has been completely restored (0.7 cm. diameter). There is free and complete evacuation of the esophagus into the stomach with no retention of contrast substance. Figure 7.

#### COMMENT

Treatment in cases of esophagospasm has swung between the extremes of conserva-

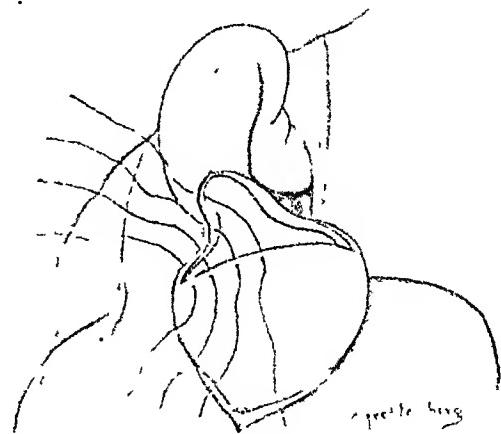


FIG. 5. Transverse incision through muscularis of stomach and suture to muscularis of lower esophagus.

tism and of operative treatment. Conservative treatment is essentially the dilatation of the esophagus at its diaphragmatic hiatus by various types of bougies, distensible dilators of the mercury, pneumatic or hydrostatic type or by direct vision dilatation through the esophagoscope (Freeman<sup>13</sup>). The lesser degrees of spasm may be overcome and the majority of cases without dilatation will respond to conservative treatment; others require repeated treatment to achieve a reasonable degree of improvement. An undetermined but probably large percentage are unresponsive to treatment, develop a permanent dilatation which eventually assume the S-shaped form which can be relieved only by surgical intervention. Moersch<sup>14</sup> reported 805 cases conservatively treated, 670 of which were traced and which include twenty-three deaths, nine due to a ruptured esophagus. Of this series 475 are listed as cures which include an undetermined percentage with continuing intermittent dysphagia. Similarly undetermined is the number of dead or incurable in the group of 135 untraced cases. It is, therefore, reasonable to conclude that less than half

of the cases treated conservatively are completely relieved and that there is a relatively high mortality rate.

essentially ineffective. The plication or excision operation is as unreasonable as applied to the esophagus as it would be if

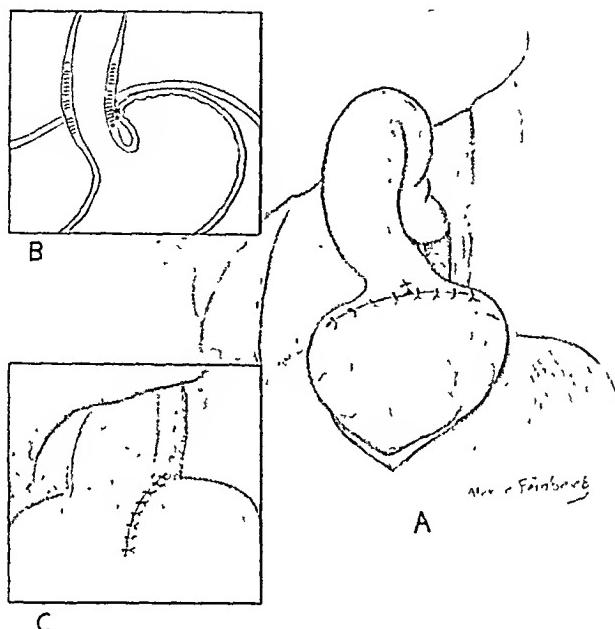


FIG. 6. Suture line protected by approximation of peritoneum of stomach to pleural layer over esophagus; diaphragm closed. Insert indicates relation of stomach to lower esophagus in its position below diaphragms.

The incidence of carcinoma developing in the dilated esophagus has been reported by Vinson and Kennedy<sup>15</sup> as three in a series of forty cases. They quote Wohlwill's cases of carcinoma developing fifteen and seventeen years after diagnosis of esophagospasm. They quote Fleiner, in whose opinion carcinoma occurs twenty-five times more often in a dilated esophagus than in cases without cardiospasm. Guisez<sup>16</sup> reported twenty-six cases of malignancy in cardiospasm. Since 42.8 per cent of carcinoma of the esophagus occurs in its lower portion (Ochsner-De Bakey<sup>17</sup>), the relation assumes an added importance.

*Choice of Operation.* Many types of operation have been done which fail to meet the indications; others palliate rather than cure and still others are too formidable to be justified. Operations such as vagectomy, sympathectomy, plication, longitudinal excision and suture, intussusception of esophagus, retrograde or transgastric dilatation have all proved

applied to the distended gut in an intestinal obstruction. Retrograde or transgastric dilatation are no more successful and have a higher mortality rate than a similar procedure through the mouth. Walton<sup>18</sup> reports three deaths in twenty-two cases. One may dismiss from consideration the esophagostomy-gastrostomy through separate abdominal and thoracic incisions. There are many adherents of the gastroenterostomy type of anastomosis between the dilated esophagus and the stomach, an operation which has several obvious disadvantages. Only a small opening may be obtained below which a spur is formed (Lambert<sup>19</sup>). This has been recognized by Gröndahl<sup>20</sup> who modified the Heyrovsky<sup>21</sup> technic (Häggstrom<sup>22</sup>) in order to overcome this objection. Such an anastomosis, however, still leaves the dilated sigmoid loop of the esophagus below the opening into the stomach and the retention of food and secretion in this loop causes a pinch-cock action on the opening. Anasto-

mosis between the lowest part of the sigmoid loop and upper stomach cannot be done since the loop is on the right and posteriorally and would not permit the necessary degree of rotation for approximation to the stomach. The results have frequently indicated an unaltered esophagus as well as continued deglutitional annoyance. In the series of reported cases reviewed, the bibliography of which has been thoroughly presented by Ochsner and De Bakey,<sup>23,24</sup> dilatation of the esophagus has persisted despite clinical improvement.

The rational surgical procedures seem to be those which directly release or remove the stricture and re-establish a free communication between the esophagus and the stomach. This may be accomplished by (1) submucous section of muscle at site of stricture (Rammstedt type) and (2) section of the stricture and esophagogastostomy (Finney type). The first type, described by Gottstein,<sup>25</sup> in 1901, was successfully performed by Heller<sup>26</sup> in 1913. He subsequently reported (1921) before the German Surgical Congress, twenty-one cases in which the patients were operated upon by various surgeons with cure in seventeen and without a death. The second type of operation advocated by Ochsner and De Bakey<sup>24</sup> has secured a clinical cure in two cases with a residual dilatation of the esophagus.

*Abdominal versus Thoracic Approach.* The few operations which seem reasonably to meet their indications require surgery of the lower thoracic esophagus. Anatomically, the gastric "cardia" and the "cardiac" sphincter are at different levels, the latter in and above the embrace of the diaphragm whereas the esophagus extends below the level of the diaphragm. Through a laparotomy incision, the depth of the operative site presents technical difficulties which are not overcome by section of the coronary ligament of the liver nor can the lower esophagus be mobilized without a possible interference with its blood supply or an accidental pneumothorax. These same difficulties are presented by a total

gastrectomy which may be justified in dealing with a carcinoma of the stomach but which should not be met in an elective



FIG. 7. Roentgenogram taken nine weeks after operation showing the lower esophagus restored to normal tone and lumen. The small pocket of contrast media below the diaphragm is in the stomach and not in the esophagus. (See arrow.)

operation. The thoracic approach, however, permits mobilization of that part of the esophagus on which plastic operation is to be done without interfering with its blood supply. The incision through the diaphragm permits the fundus of the stomach to be brought into the operative field and any type of operation such as a Rammstedt or Finney or Billroth I type of operation as is performed on the pylorus, may be done at the gastroesophageal portion with ample room and easy accessibility for the most exacting technic. The ease of closure of the thoracic wound is in itself an obvious advantage over the difficulty of closing a sufficiently large, upper abdominal incision. The pneumothorax exists only for the duration of the operation and is not followed by a distressing train of post-operative symptoms as in an extensive

laparotomy. One who has performed major abdominal surgery on the upper portion of the stomach, will be impressed by the simplicity and ease of the thoracic approach.

#### SUMMARY

1. The case reported has been cured symptomatically and the lower esophagus has resumed its normal diameter and tonicity.

2. A larger percentage of patients with esophagospasm should be operated upon before extreme dilatation and atony occur. Conservatism and palliation in a large number of patients require continuous treatment to accomplish semi-invalidism. Carcinoma follows dilatation of the esophagus twenty-five times as often as in the undilated esophagus.

3. The type of operation should be limited to those which relieve or remove the stricture, preferably through a transthoracic approach.

4. Collaboration of the abdominal surgeon with the thoracic surgeon may effect an increasing number of complete cures with a decreasing mortality rate.

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# SOLITARY DIVERTICULITIS OF THE CECUM\*

IRVING BUSCH, M.D.

Associate Surgeon, Beth Israel Hospital

AND

LOUIS FRIEDFELD, M.D.

Clinical Assistant Cardiologist, Jewish Hospital

NEW YORK, NEW YORK

THE most common site of an acute surgical abdominal condition is the right lower quadrant. While it is conceded that the surgical disease most frequently found in this region is acute appendicitis, one is occasionally confronted with surprising nonappendicular lesions. One of these is inflammation of a solitary diverticulum of the cecum.

Preoperatively, our case of solitary diverticulitis of the cecum so closely simulated acute appendicitis that we were prompted to study other reports of this interesting condition. After a survey of the literature, the need for recognition of this condition at laparotomy was apparent. The surgical treatment of diverticulitis of the cecum is relatively simple. Needless drastic surgical procedures for other conditions with which it may be confused should be obviated.

## CASE REPORT

R. L., a white married woman of twenty-five years, entered Beth Israel Hospital on April 5, 1940, complaining of pain in the right lower quadrant for the previous twelve hours. The patient was perfectly well until the day before admission to the hospital when she noted some sticking pain in the epigastrium which lasted for several hours and then completely disappeared. The patient slept well during the previous night but awoke in the morning with severe pain in the right lower quadrant. During the course of the day the pain abated and at the time of her admission to the hospital the pain was considerably less than at the onset. There was no nausea or vomiting. No anorexia was present. There was mild constipation which was effectively relieved with an enema.

Except for pneumonia during childhood, her past history was irrelevant.

Physical examination revealed a well developed and nourished white female housewife

who did not appear acutely ill. The temperature on admission to the hospital was 99.8°F., pulse was 110, respirations 26. Blood pressure was 138/70. Physical examination was otherwise negative, except for the abdominal findings. The abdomen was not distended. There was moderate tenderness on palpation over a point just lateral and below McBurney's point. Moderate rigidity was present. No masses were palpable. No other abnormal abdominal findings were present. Pelvic examination revealed moderate tenderness in the right fornix; otherwise it was negative.

The urine showed a trace of albumen and occasional white blood cells. Specific gravity was 1.010. No other abnormal findings were present. The blood count before operation showed 11,000 leucocytes, of which 79 per cent were polymorphonuclear, and 21 per cent lymphocytes. The Wassermann, Kline and Kahn reactions were negative.

A preoperative diagnosis of acute appendicitis was made and a laparotomy was done shortly after admission to the hospital. On opening the abdomen, the appendix was found to be slightly congested but otherwise normal. Just to the outer side of the anterior tenia of the cecum, opposite the base of the appendix, was an indurated pinkish-gray, inflammatory mass, measuring about 2.5 cm. in diameter. During manipulation, a fecolith could be felt slipping from this mass into the lumen of the cecum. A diagnosis of diverticulitis was made and an excision of the inflamed diverticulum was done. Two layers of chronic catgut interrupted sutures were used to effect a closure of the cecum. The appendix was removed. The wound was closed without drainage.

Pathological report by Dr. Alfred Plaut: Grossly, there was a slightly hyperemic, thin appendix, 8 cm. long. There was a roughly triangular, flat piece of tissue, with borders measuring 3.5 by 3 by 2.5 cm. The surfaces were pinkish-yellow and covered with adhesions. In the center of one surface was an ovoid crater, 8 by 6 by 4 mm. deep. Its edges

\* From the Surgical Service of Beth Israel Hospital, New York, New York.

were overhanging and the lining of the crater was smooth and glistening. Separated from this crater by a fold of tissue was a smaller, more irregular area. At one angle of the specimen was a round opening into which a probe could be passed for a distance of 8 mm. This tract was lined by velvety mucosa. Microscopically, the picture was that of a severely inflamed pseudodiverticulum. The muscle coat was interrupted by wide gaps, or one might say only remnants of the muscle coat were found in the wall of the structure. The outer layers were formed by severely inflamed fatty tissue and connective tissue into which single muscle bundles protruded. The mucosa and submucosa, as far as preserved, were not unusual. Lymph follicles were very large. The muscularis mucosae in places seemed unusually thick. There was a severely inflamed lymph-node.

No inflammation was seen in the sections from the appendix. The subserous tissue in places was edematous. There was beginning involution. Diagnosis: Inflamed false diverticulum; appendix in involution.

The postoperative course was completely uneventful, the patient being discharged from the hospital on April 18, 1940. The day before her discharge from the hospital, the colon was investigated by means of a barium enema to determine the presence of other diverticula. This showed no obstruction or delay in filling of the colon from the rectum to the cecum. There were no diverticula of the colon visualized.

The patient was followed up and last seen in July, 1941. There were no abdominal complaints since the operation.

Although cecal diverticula as part of multiple diverticular involvement of the colon are common, reported instances of solitary diverticulitis of the cecum are rare. Besides our case, a careful survey of the literature revealed twenty-seven proved cases of solitary cecal diverticulitis.

In the reported cases of this condition there was equal distribution in both sexes. Twenty-three of the total number were distributed between the third and the sixth decades. The youngest patient was nineteen and the oldest sixty-nine.

Pain in the right lower quadrant, accompanied by tenderness and rigidity, occurred

in almost all cases. Occasionally, a mass could be felt in the right lower quadrant. Nausea and vomiting were present in a small percentage. The temperature was normal or a low grade fever existed along with either a normal or a slightly elevated leucocyte count. The incidence of the clinical findings are listed in Table I.

TABLE I  
TWENTY-EIGHT CASES

Pain.....	27
Tenderness.....	21
Rigidity.....	17
Mass.....	10
Nausea.....	5
Vomiting.....	4
Rebound tenderness.....	2
Rectal tenderness.....	1
Diarrhea.....	1
Chills.....	1

*Pathology.* Most commonly, diverticula of the gastrointestinal tract are classified as true or false. The former include those in which the diverticulum is made up of all the coats of the intestinal wall. The false present those cases in which there is an outpouching of the mucosa through a weak spot in the intestinal wall so that the diverticulum lacks the muscular layer, wholly or in part.

A diverticulum being a bottle-necked structure, there is a tendency to stasis of fecal material. With the increase of stasis, there is greater water absorption with the resultant formation of a fecolith. The contents of the cecum being more fluid than that of the more distal part of the large intestine, fecolith formation is ordinarily less likely to occur. Because of the lack of muscular fibers in the false type of diverticulum, the necessary force to expel the trapped fecal material is lacking. The presence of a trapped fecolith in a diverticulum leads to irritation and infection resulting in diverticulitis.

Diverticulitis of the cecum may be acute or chronic. The acute type may be localized to a small area of the cecum of variable size, forming a thick inflammatory swelling. Progression of the localized process may result in either a perforation with general peritonitis or a localized abscess.

The localized abscess may progress and rupture into the bladder, forming a colovesical fistula, or it may rupture into the general peritoneal cavity. The acute diverticulitis may become chronic. The chronic type may eventually produce a pericolitis with adhesions to the neighboring organs. Another sequel of chronic diverticulitis is intestinal obstruction.

Microscopically, the picture varies with the type and the stage of the inflammatory process. The submucosa shows the greatest reaction in the beginning with progression and extension to the peritoneal coat. The acute stage shows a predominance of polymorphonuclear cells. The chronic type shows the presence of lymphocytes and marked increase of fibrous tissue.

**Prognosis.** There were three deaths in the reviewed series. Two followed extensive resections and anastomoses; the third was a case of a perforated diverticulitis that developed a generalized peritonitis. More than half of the cases had extensive surgery done. Some of these cases could have been treated by simpler procedures if the underlying gross pathological condition had been recognized at the operating table. This would have reduced the postoperative morbidity.

#### DISCUSSION

Diverticulitis of the colon occurs most commonly in the sigmoid and has frequently been called "left-sided appendicitis." However, the converse must be considered, that the picture of true appendicitis may be simulated by cecal diverticulitis.

With the recognition of cecal diverticulitis, and its gross differentiation from carcinoma, tuberculosis and other conditions with which it may be confused, a simple surgical procedure usually suffices. Experience has shown that simple excision of the inflamed diverticulum and suture of the intestinal wall is adequate. The treat-

ment of such complications as abscess, fistulae or obstruction must be individualized.

#### CONCLUSIONS

A case of solitary diverticulitis of the cecum is presented.

A survey of the reported cases demonstrates the need of proper recognition of this condition at the time of operation.

Simple surgical procedure is usually indicated.

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# FATAL OBSTRUCTIVE UROPATHY RESULTING FROM URETHRAL CARUNCLE\*

## CASE REPORT

LEONARD WALLENSTEIN, M.D.

BALTIMORE, MARYLAND

URETHRAL caruncle or vascular tumor of the meatus was first described by Samuel Sharp in 1750. Since then investigators have devoted much attention to this affection. The growth, usually seated upon the lower half of the external orifice of the urethra, is attached by a pedicle on a broad base which sometimes extends into the urethral canal with a raspberry appearance. Histologically, the tumor is made up of connective tissue and hypertrophied papillae with numerous dilated vessels, covered by pavement epithelium.

The clinical history of a urethral caruncle is striking, the majority causing exquisite pain during urination. Bleeding occurs on slightest trauma because of the many thin-walled vessels in the tumor. The treatment of this condition is either fulguration with the electrospark gap or excision well beyond the broad base. Subsequent dilatation of the urethra is important.

Search of the literature fails to reveal the report of any cases of caruncle which resulted in obstruction of the urinary tract, stasis, infection, uremia and fatal termination.

## CASE REPORT

This patient (F. H.), a fifty-six-year old, widowed, white female, was sent to the West Baltimore General Hospital December 20, 1940. The family physician had stated that the patient had a large mass easily palpable in the lower portion of the abdomen. On admission, the patient was extremely weak, stuporous and quite ill. The chief and only complaint was weakness which had become progressive in the past three years. Review of systems revealed

only a few significant facts. The patient's appetite had fallen off considerably in the last six months. Her bowels moved sluggishly. Menopause had occurred uneventfully nine years ago at age of forty-seven. The only urinary symptom noted was a slight increase in the frequency of urination, with a nocturia of one to two times in the past three years.

Physical examination revealed the patient to be a fairly well developed, sallow complexioned, white female lying in bed, somewhat drowsy and irritable. The skin hung loosely. The head and neck revealed no abnormalities. Percussion note of chest was resonant bilaterally. Breath sounds were vesicular except for an occasional crackling râlc in the right axilla. The heart sounds were clear except for a faint systolic murmur at the mitral area. No cardiac enlargement was noted by percussion. Blood pressure was 180/86. A large mass was present in the right lower abdomen, extending to the umbilicus, very firm, smooth surfaced, not lobulated and not tender. The liver and spleen were not palpable and there was no edema of the lower extremities. Neurological examination was entirely negative. Pelvic examination revealed a small red raspberry-like tumor obscuring the urethral orifice. The vaginal vault was deep and the patient was not co-operative. The large mass felt abdominally was bulging into the vaginal wall.

Admission laboratory data were: *Urinalysis*: yellow, cloudy; specific gravity, 1019; sugar, negative; albumin—3 plus; microscopic (high power field), 2-5-red blood cells; 2-5-white blood cells; occasional granular cast; *intravenous phenosulfophthalein*, 2 per cent total excretion in two hours; *blood count*: hemoglobin—62 per cent (Sahli); red blood count, 2,580,000; white blood count, 10,000; polymorphonuclears, 96 per cent; lymphocytes, 4 per cent; *blood urea*: 142.5 mg. per cent; *Wassermann test*: negative; *blood proteins*: 6.8; albumin 3.8; globulin 3.

\* From the Department of Genito-Urinary Surgery and Hospital, Baltimore, Maryland.

The patient was placed on a régime of intravenous 10 per cent glucose in water with sodium Ringer lactate. Blood transfusions of

dilated forming a large sacculation. There was no vesical neck obstruction and the urethra was easily distensible. The cystoscope was with-



FIG. 1. Cystogram (anteroposterior view) showing large dilated bladder with sacculation at dome.

250 cc. each daily were given. When the patient was ordered catheterized, prior to pelvic examination by the service consultant, it was reported by the nurse that the usual female catheter could not be introduced into the urethra. On close inspection it was found that the caruncle was completely obstructing the urethral orifice. The patient was taken to the cystoscopic room where after routine preparation it was definitely determined that the caruncle was blocking the urethral meatus and had encircled the orifice except for a pin-point opening at its superior portion. First a probe, then Hegar dilators were inserted. Finally, the caruncle was grasped with Allis forceps and removed with the electro-surgical loop in a circular fashion down to the muscular coat of the urethra. A No. 21 French, Ravisch cystoscope was then easily inserted through the urethra into the bladder and the bladder slowly decompressed of 1,800 cc. of urine, the last 800 cc. of which was pink and muddy in appearance. The bladder was irrigated with several liters of sterile water. The ureteral orifices were visualized and were normal in position but dilated. The dome of the bladder was markedly trabeculated and the right lateral superior portion of the bladder was



FIG. 2. Cystogram (oblique view) sacculation at superior portion and reflux of dye into dilated, kinked ureters.

drawn and a No. 25 mushroom catheter was inserted into the urethra, and the patient returned to her bed in fair condition.

The blood pressure following this procedure fell from 176/82 to 126/80 in a period of six hours and then rose to 150/76 where it maintained itself for a period of days. With further intravenous glucose and blood transfusions the patient's course seemed slightly improved. The urea dropped from an admission level of 142.5 to 105 where, however, it remained fixed. On January 9, 1941 the patient was thought strong enough to permit the taking of cystograms. Using 250 cc. of 6 per cent sodium iodide a large sacculation on the right posterior surface of the bladder was visualized. (Figs. 1 and 2.) In addition marked tortuosity, kinking and dilatation of the ureters were noted. Three days later the patient again began to show signs of drowsiness and irritability. The quantity of urine voided by the patient until this time was between 12 and 1,500 cc. daily. This began to decrease and the urine became grossly bloody in appearance. Blood urea rose to 116 mg. per cent. On January 12th the patient became unconscious, pulse was feeble, rapid, and

despite supportive and stimulative therapy exodus took place on January 13th at 12:40 A.M. Permission for autopsy was obtained and the



FIG. 3. Autopsy specimen; markedly hypertrophied bladder with dilated kinked ureters and dilated kidney pelvises.

most important findings were, of course, in the urinary tract. (Fig. 3.) The urethra was patulous, mucosa injected. On microscopic serial section there was no evidence of malignancy or stricture of the urethra, but there was inflammatory reaction at the point where the caruncle had been removed. The bladder was markedly hypertrophied and dilated. The bladder wall measured 1.8 cm. in its thickest diameter. There was a wide pouch extending from the right posterior surface. The mucosa revealed marked inflammatory and ulcerative changes. The ureters were bilaterally dilated, kinked and thickened, microscopic sections showing severe ureteritis. The kidneys had widely dilated and thinned out pelvés, with scattered cortical abscesses. Microscopic diagnosis: bilateral pyelonephritis with cortical abscesses. Significant facts in the remainder of the examination were atheromatous changes in the aorta and a moderate sclerosis of the coronary vessels. Section of the caruncle removed from the urinary meatus revealed villus-like surfaces of epithelium with papillary hyperplasia, having a uniform base line. There were many endothelial-lined small vessels present in the stroma.

#### COMMENT

The fact that this abdominal tumor might be a hugely distended bladder was not given immediate consideration for several reasons: (1) The patient gave no significant urinary history except slight frequency; (2) a voided specimen of urine (50 cc.) was obtained on admission. Most unusual was the fact that the mass was not tender and freely admitted the palpating hand with pressure, the patient showing no discomfort. A similar bladder distention in the male patient due to vesical neck obstruction causes distress which one cannot pass over. It was, therefore, an initial impression that this might be a large ovarian tumor obstructing the right ureter and so causing a surgical hydronephrosis with uremia. Only after the caruncle had been found to prevent catheterization, the true nature of the mass was discovered. Cystoscopic findings: (1) Hypertrophy of the bladder with marked trabeculation and sacculation; (2) no vesical neck obstruction and no urethral stricture, left only the caruncle at the meatus as a satisfactory explanation for the obstructive uropathy.

#### CONCLUSION

In considering the diagnosis of any low abdominal mass, whether or not it be tender or centric, the bladder must be kept in mind. Before any satisfactory pelvic examination can be attempted the bladder should be emptied. The importance of thorough examination of the urinary meatus both as to appearance and function whenever a patient presents a low abdominal tumor, is well borne out here. The severe irreparable damage to the upper urinary tract over a period of several years brought a fatal termination in this case despite removal of the obstructing factor.

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# Bookshelf Browsing

## DR. GORDON S. SEAGRAVE IN BURMA

THE following excerpts are from a letter\* written by Dr. Gordon S. Seagrave (now Major Seagrave) from Delhi to his wife. Dr. Seagrave was a medical missionary in Burma at the time of the Japanese invasion. When Burma was evacuated, the author of this letter accompanied General Stillwell into India.

"We were ordered to follow the Chinese Sixth Army down to Loilem and left some time in February. When we got there they told us we would have to serve the whole army, not just one division. We went back and set up a base hospital in Loilem—bamboo huts and wards on a hill out of town, a lovely joint. . . .

"Dr. Geren, Tun Shein and I, with Ko Nyunt and a Chinese college boy, Low Wang, and twelve nurses started off for Pyinmana. We got to Case's [Baptist Missionary Brayton C. Case, founder of an agricultural school at Pyinmana] place while he was away late at night. The Friends' Ambulance Unit arrived almost immediately and while they went off for casualties we set up. They got back after we had managed to get two hours sleep and from then on we worked steadily, with only two hours rest, for 36 hours. Case moved us off to a child welfare house in town. We had just begun operating there when a lot of Jap planes went over. . . .

"While we were operating after the bombing—I had four operating tables going at once with nurses finishing the operations after I had done the most essential part, and Koi [one of the nurses] operating on her own—General Stilwell came in and watched us without our know-

ing he was there. As soon as he got to Maymyo he sent down the only U. S. Army medical man he had in Burma, a dentist named Captain (now Major) Donald M. O'Hara, and telegraphed Chungking to send down an abdominal surgeon trained at the Mayo Clinic, a Captain John Grindlay, to work with me. Grindlay, after having Koi, Kyang Lewi and Maru Bauk assist him at various particularly bad cases, adopted the whole crowd, and to this day tells everyone they are the best trained nurses he ever saw. . . .

"My first brain cases, etc. were really interesting. The first one had a bullet enter the top of his head and go three inches into his brain. I trephined a huge opening in his skull, opened up the dura mater, washed out a lot of shattered brains and put in a vaseline gauze drain. That night we had to move and took him along with us to a bungalow on a hill. Every time bombers came over, this patient got up and ran half a mile. After five days, during which he had no fever and was walking around everywhere—drain out—we had to send him back.

"Then one day they brought in another just like him, but with lots of other wounds all over his body. I was sure he would die on the table, and there were lots of others who needed immediate operation so I told them to carry him out and let him die in peace. After all the other cases were done, one of the nurses wanted to know what I was going to do for the patient they had dumped behind the kitchen, so I said that if he was still alive to bring him in. I did his brains the same way, fixed up all his other wounds,

\* Through the courtesy of Mrs. Gordon S. Seagrave and *Time Magazine*, who published the above in their July 20th issue, we are able to offer our readers this most interesting letter.

and three days later we shipped him off in good condition.

"We had loads of variety. There were some quiet spells, but usually we began operating at midnight and on until 8 or 10 in the morning, then the nurses and I would take all the bloody operating stuff to a stream, wash it out, and Emily would resterilize it for use that night. I got four scratches, two on each foot, dropping boxes on myself while moving and then getting streptococcus sloughs from infected patients' blood and pus dropping onto my feet, and they took forever to heal. Yesterday was the first day I didn't have to have a dressing on my right foot for three months.

"We kept moving back. . . .

"About two days later, they decided to abandon Burma and we started off with General Stilwell's crowd. We drove about 150 miles west in the trucks and jeeps and then had to abandon them one by one if they got stalled even for a few moments. We were ordered to save out only what each one thought he could carry up the Chin Hills and abandon the trucks. I knew we would have to take care of all the sick in the company of

105 who followed General Stilwell out, so I ordered each nurse to carry some first-aid articles in addition to her own stuff. So they each took out two jackets, two longyiis and a sheet. They had one blanket to each three. We had 19 nurses and seven Friends' Ambulance Unit men and seven of the rest of us, by this time.

"I pretty nearly died that first day, it was so ghastly hot. Next day, and for three more days, we had to march down the middle of a stream. Sand got into our shoes and socks and my sores got four times as big as they had been. Then we had three days on rafts made of rotten bamboos. My bed was six inches under water. Then we crossed the Chindwin and started up and down some awfully steep hills, some 7,000 feet high. I had had malaria every couple of weeks since December and the day we reached the Assam border I couldn't have walked another step. When we reached civilization I was down to 50% hemoglobin, had lost 35 pounds and my legs were swollen to the knees. . . .

"I hope you approve of my joining the Army."



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